ORAL DELIVERY FORMULATION

Related Applications

This application claims the benefit of priority under 35 U.S.C. Section 119 to U.S. patent application entitled "Oral Delivery Formulation", filed December 15, 1997 and U.S. patent application entitled "Oral Delivery Formulation", filed February 4, 1998. Serial numbers presently not known. This application also claims the benefit of priority under 35 U.S.C. §120 to U.S. Patent Application entitled "Oral Delivery Formulation", filed April 4, 1998, serial number presently not known.

Background of the Invention

Current orally delivered drugs are formulated in either solid (i.e., tablet, capsule or granules) or liquid (i.e., solution, suspension or emulsion) form. Solid dosage forms are conventionally the dosage of choice as they are typically more stable, less expensive to manufacture and have achieved general acceptance by consumers. The manufacture of solid dosage forms typically involves the processing of the drug with suitable excipients in order to produce a freely-flowing powder. The type of processing and excipients chosen to manufacture the powder can be altered to provide desired effects such as controlled release of the drug. Once processed, the powder can be directly packaged into sachets, compressed into tablets or filled into capsules. Tablets can further be coated in order to improve palatability or provide controlled release of the drug.

Oral liquid dosage forms are primarily used by the pediatric population and those who experience difficulty in swallowing. Liquid dosage forms are available orally as solutions, suspensions or emulsions. These liquids often contain colorants and flavorings in an attempt to increase palatability and patient acceptance.

Many patients, however, are unable to adequately ingest either solid or liquid dosage forms. To address this problem, health care providers often crush solid dosage forms and disperse them in a semi-solid medium (e.g., applesauce, pudding). However, when tablets or capsules are tampered with, the drug release kinetics of the pharmaceutics are altered. This can result in dose dumping and serum concentrations which are non-optimal and can be dangerous.

There are a number of drug administration and patient compliance issues peculiar to the geriatric market, which result from hard to swallow tablets, unpleasant taste and texture, frequent

dosing regimens or unfavorable side effect profiles of certain drugs. Current tablet and liquid dosage forms do not address the needs of the elderly patient. Physical limitations prevalent amongst the elderly hinder their ability to swallow traditional dosage forms and to self-administer medication (e.g., arthritis, tremors associated with neurological disorders, visual impairment, and memory problems). Physical limitations present in this age group include difficulty in swallowing due to dehydration, "mouth breathing", and esophageal lesions. Chewing also is difficult due to reduced bulk and tone of oral musculature as well as loss of or degradation in the quality of their teeth.

Other patient populations present drug administration and patient complianee issues. These include pediatrie patients (i.c. children about 5 years old or less), certain oncology patients, late-stage AID patients, post-surgieal patients and patients who other advanced disease states which are physically debilitating.

There remains a need for dosage formats which are eompatible with sueh populations and which addresses the physical and physiological limitations of these populations. There remains a need to provide dosage formats which can be administered to patients which experience difficulty in swallowing solids (tablet) and liquids.

In attempts to solve some of the above issues, different formulations of nano- or micro-granules have been reported (see, US 5,618,527). These formulations consist of spherically-shaped particles in either a liquid or a tablet form, in which the particles are not greater than 125 μm in diameter to avoid the sensation of grittiness. Also, the particles need to have smooth edges. These requirements severely limit the flexibility of the drug manufacture and delivery.

Similar attempts to reduce the sensation of grittiness was described by using a blend of a gritty drug with a seedy fibrous fruit (US 5,102,664). In this eombination the seedy fibrous fruit texture masks the grittiness of the drug. The problem of grittiness also is evidenced in certain topical formulations. Topical formulations whieh contain particles of drugs (or particles eontaining drugs) have an unpleasant gritty feel when applied to the skin.

There exists the need for a drug delivery format which is adaptable to patient populations that have trouble ehewing and swallowing. There also exists a need for a drug delivery system which is adaptable to all formats, ineluding oral, topical, injeetable, and other delivery formats. There also is a need for a drug delivery system that can permit adjustment of the release profile of the drug. Various aspeets of the present invention address the foregoing needs.

Summary of the Invention

The present invention provides novel methods and products for the manufacture and use of novel drug delivery systems.

According to one aspect of the invention, a composition is provided. The composition is a plurality of discrete, substantially flat flakes, each having an average length, an average width and an average thickness, wherein each of the length and the width are at least three times the thickness, wherein a longest dimension of each flake is between 100 nanometers and 5 millimeters, and wherein the flakes comprise a drug or a nondrug nonnutritional active agent. In one embodiment, each of the flakes has a surface area, and the ratio of the surface area to the thickness is at least 25 units ^{2}:1 unit. In another embodiment, the longest dimension of each flake is between 10 microns and 1 millimeter. In still another embodiment, the ratio of the surface area to the thickness is at least 100 units ^{2}:1 unit.

The drug can comprise a very small amount of the flakes or it can comprise a very large amount of the flakes by weight. Thus, the drug can comprise between 0.001% and 100% by weight of the flakes. In certain embodiments, the drug is at least 0.05% be weight of the flakes. In important embodiments, the drug is at least 5% by weight of the flakes. In other important embodiments, the drug is at least 10%, at least 25%, or at least 50% by weight of the flakes.

The drug can be embedded within the flakes or the drug can be coated on the flakes. If the drug is embedded within the flakes, then the flakes can be made entirely of the drug or the drug can be dispersed throughout all or a portion of the flakes. If the drug is dispersed throughout the flake, then the drug can be a component of the flake, can be contained in discrete microparticles dispersed throughout the flake, can be in one or more layers comprising the flake or can be physically and/or chemically retained within a flake which comprises a porous matrix. The drug also can be coated on a surface of the flakes. The coating can be an even continuous coating or can be a noncontinuous coating. The drug can be contained in microspheres which are coated on the flakes. The drug also can be coated directed onto the flakes or can be attached covalently or noncovalently to the flakes by linkers.

In one important embodiment, the flakes further comprise a coating on the flakes. This coating can in some embodiments separate the drug from the environment. The coating can be an enteric coating covering the flake. Other coatings are described below.

The flakes can be made of any one of a variety of materials, polymers or non-polymers, discussed in greater detail below. The flakes can comprise natural polymers. In some

embodiments, the flakes are at least 25% by weight of the natural polymer. The flakes also can comprise a synthetic polymer. In many embodiments, the flake is at least 5% by weight a nonfood. In most embodiments, the flake is at least 25%, at least 50% and at least 75% by weight of a nonfood. In other embodiments, the flake can comprise a drug uptake enhancer. A drug uptake enhancer is a material which, when it is administered together with the drug, facilitates uptake of the drug in the environment in which the drug is delivered. Drug uptake enhancers are well known for a variety of drugs and are approved by the FDA.

According to another aspect of the invention, another composition is provided. The composition is a plurality of discrete, substantially flat flakes, each having an average length, an average width and an average thickness, wherein each of the length and the width or at least three times the thickness, wherein the longest dimension of each flake is between 100 nanometers and 5 millimeters, and wherein each flake comprises a porous matrix. The pores are large enough to accommodate a drug or a nondrug, nonnutritional active agent. In this aspect of the invention, the composition can further comprise a drug or active agent. The flake in some embodiments is at least 5%, at least 10%, at least 25%, or at least 50% a nonfood. Important embodiments such as dimensions, ratios, percent drug contained within the flake, and so on are as described above.

According to another aspect of the invention, a pharmaceutical preparation is provided. The pharmaceutical preparation contains any one of the compositions as described above, and a pharmaceutically acceptable carrier. The pharmaceutical composition contains an amount of the drug effective for treating a condition treatable by the drug. In certain embodiments, the pharmaceutical preparation is formulated as an oral dosage form. The oral dosage form can be a semi-solid food. In another embodiment, the pharmaceutical preparation is formulated as a topical preparation. The topical preparation can contain an agent that is non-suitable for oral ingestion. In still another embodiment, the pharmaceutical preparation is formulated as an implant. In yet another embodiment, the pharmaceutically acceptable carrier is a semi-solid. These forms can be controlled release forms, delayed-release forms or sustained-release forms. The semi-solid can be a hydrogel or a food. The flakes can be coated as described above. They also can be coated with a taste-masking composition.

According to still another aspect of the invention, a method is provided for treating a subject having a condition. The method involves administering to a subject in need of such treatment an amount of a drug effective to treat the condition, wherein the drug comprises a plurality of flakes. In important embodiments, the flakes comprise any one of the

pharmaceutical preparations as described above. In another important embodiment, the drug is administered orally. In another important embodiment, the subject has a condition making it difficult to swallow. The subject can be selected from the group consisting of a geriatric subject, a subject with cancer, a subject who is post-surgically recovering, an infant, a child five years old or less, or a late-stage AIDs subject.

According to yet another aspect of the invention, a method is provided for preparing a pharmaceutical preparation. The method is an improvement to the known methods for forming pharmaceutical preparations by incorporating a drug within or coating a drug onto a particle, the improvement comprising incorporating the drug within or onto a flake. In important embodiments, the flakes are as described above.

According to another aspect of the invention, a method is provided for preparing a pharmaceutical preparation. The method involves incorporating a drug into or upon a plurality of flakes. In one embodiment, the flakes are formed first, and then the drug is coated onto, or allowed to penetrate into, the flakes. In another embodiment, the drug is incorporated into the flakes by forming the flakes in the environment of the drug.

The drug-incorporated flakes (DIF) may be administered in a variety of media, including liquid, tablet and food-feedable basis. The DIF provides all the benefits for controlling the release kinetics of the drug available in conventional drug delivery methods. In addition, it may alleviate many of the shortcomings of nano- and macro-granules in terms of size and manufacturing constraints.

The invention has been described in this summary in connection with drugs. Drugs are defined specifically in the specification as excluding nontherapeutic doses of nutritional supplements. The drugs typically are not nutritional supplements such as vitamins and minerals (i.e. nonnutritional drugs). The agent carried by the flakes of the invention, however, need not be a drug. The agent can be a nondrug active agent such as an insect repellant, a sunscreen agent, a pesticide, etc. Classes of nondrug agents are described below.

The invention also contemplates both food and nonfood flakes. In most embodiments of the invention the flake is a nonfood such as a synthetic polymer for carrying the drug or other active agent. It is an embodiment of the invention, however, that the flake can be a food such as an oat flake or a grape nut flake. When the flake is a food, then the drug either is not a nutritional supplement, or, if it is a nutritional supplement, it is present at therapeutic levels which are above nutritional supplement levels of the prior art. Thus, the invention intends to

exclude the prior art nutritionally supplemented food flakes such as fortified oatflakes and fortified cereal flakes.

It is known that a variety of drugs have enhanced therapeutic effects due to improvements in drug delivery when delivered together with a drug uptake enhancer. Such enhancers can be included with a drug in a single flake or can be provided separate from the drug carried on its own flake. Thus, the plurality of flakes can be mixtures of flakes, some containing a drug and some carrying nondrug component, that act as an adjunct to therapy. One important example of this is flakes which have anti-constipation properties. Many drugs cause constipation and many patients such as geriatrics are chronically constipated. Flakes which are a mixture of drugs and anti-constipation agents are useful for such patient populations.

The present invention also provides a spoon-feedable drug delivery vehicle. The vehicle includes a viscose base having a consistency capable of being spoon-feed. The viscose base may be food or non-food. Particles comprising a drug and, optionally, a synthetic or natural carrier are added to or mixed into the viscose base. The particles may have any suitable size and shape, such as by way of example, spherical, oblong, and flake-like particles as described above. The drug may be provided premixed with the base, or it may be supplied separately from the base for mixing just prior to consumption.

The spoon-feedable drug delivery vehicle also can be a nutritionally fortified delivery vehicle (NFDV). The NFDV has a semi-viscose or semi-solid consisteney which may be readily spoon-fed. This base may be supplied in a unit dose package in a variety of flavors and compositions. The NFDV provides a spoon-fed base for administration of drugs which addresses the difficulties in some patient populations intolerant of orally delivered medication. In addition, it can provide necessary dietary nutrients and/or fiber.

Detailed Description of the Invention

It has been observed previously that spherical or granular particulates leave a gritty sensation in the mouth which can be unpleasant to the patient when administering micro-granules. The present invention has recognized that drugs which are incorporated into a flaked delivery vehicle possess enhanced mouth feel by eliminating or reducing the gritty feel characteristic of the prior art particles. It is anticipated that the flakes of the present invention will be better tolerated by the patient, leading to more complete dosages and higher compliance when used for oral delivery.

A flake is a substantially flat, thin layer or unit and thus possesses a dimension which is substantially less than the other two dimensions. The flake may be substantially planar or similar to curvilinear.

In a preferred embodiment, the flake has a size of between 10 and 500 microns along its longest dimension. The flakes preferably are free flowing. The flakes can be relatively uniform and consistent in size and morphology or can be a mixture of flakes of different sizes and morphologies.

The invention involves in one aspect the delivery of drugs in or on such flakes. A "plurality" of flakes is referred to. A plurality means greater than 100. In important embodiments, the plurality is greater than a thousand, greater than ten thousand and even greater than one hundred thousand.

The flakes can be non-porous or porous. The flakes can be made entirely of the drug or can be as low as 0.001% drug-containing. Thus, the drug may be combined with any of the variety of normal excipients, binders, fillers and the like and formed into a solid flake. The excipients may be non-polymers or polymers. In one important non-polymer embodiment, which is merely exemplary, the flake is a "fused" flake. In a "fused" flake, a drug, a carrier, or both are melted and recrystallized to form a crystalline matrix of the drug and/or carrier. In a totally fused flake, both the drug and the carrier are melted and recrystallized. In a partially fused flake, only the carrier is melted and recrystallized, thereby capturing the drug in the crystalline matrix of the carrier. Sterols are particularly suited for melting and recrystalization. For example, various cholesterol-type compounds, including cholesterol acetate may be used. Compounds such as palmitic acid also can be used. Detailed parameters about forming "fused" drug delivery materials are disclosed in U.S. patent numbers 4,748,024, 4,892,734 and 5,039,660, the entire disclosures of which are incorporated herein by reference. These patents illustrate that virtually any amount of drug and carrier, including no carrier, can be used in the formation of such materials.

The excipient also may be a polymer. The types of polymers that may be used are described in great detail below. The polymers are substantially coextensive with the materials which are used in connection with making nano- and microparticles or spheres (hereinafter "microparticles"). Such polymers further include bioadhesives which are particularly suited for oral delivery methodologies, as is described and known in the prior art. Using such polymers, nonporous flakes can be manufactured or porous flakes can be manufactured. The drug can be

loaded into the flake during the manufacture of the flake or may be added to the flake after the manufacture of the flake, by causing the drug to be absorbed into or adsorbed onto the flake or by coating the drug onto the outside surface of the flake. In the various methodologies used for manufacturing microparticles, it is shown that a drug can be physically entrapped within the polymer, chemically bound within the polymer (covalently or noncovalently) or physiochemically entrapped within or bound to the polymer. The present invention does not involve the use of new polymers and the like, but instead involves the use of known technology for drug delivery with the exception that the materials are manufactured and fashioned in the form of a flake rather than in an amorphous or spherical particle.

Also as well known in the prior art, the flakes can be coated with materials. Such coatings can be enteric coatings for permitting the flakes to pass through the stomach and into the intestine prior to releasing the drug. Such coatings also can be taste-masking coatings, such as is described in U.S. patent 5,084,278 and the patents cited therein, the disclosure of which is incorporated herein by reference. The present invention does not present new coating technology, but instead the flake particles of the present invention can be coated in the same manner as the prior art particle and microparticle delivery technologies. The coatings may be made from the same material as the flake or from different materials. The coatings, in general, are adapted to protect the drugs contained in the flakes, to provide advantages to the flakes in their environment of use (such as by permitting the flake to pass through the stomach), to cause the flakes to be less likely to aggregate with one another and the like.

The release dynamic of drugs from the flakes can be controlled in a conventional manner, just as the release profile of drugs is controlled in other similar technologies such as in a particle-based or polymer-based delivery systems. According to the invention, therefore, flakes can be manufactured so as to control and/or vary parameters such as size, morphology, materials and coatings to influence release of drugs from the flakes. Controlling such parameters can achieve drug release profiles as desired, including delayed-release, timed-release, and sustained-release. One advantage of the flakes according to the invention is that the release profile can be made more uniform, because, unlike for a particle or sphere, the surface area of a flake is relatively constant as it erodes. In any event, virtually any release profile can be achieved using technologies which are well known to those of ordinary skill in this art.

The flakes can be manufactured in virtually any size, although preferred sizes are as described above. A principal characteristic of size which affects the length of time over which a

drug is released is the thickness of the flake. The thicker the flake, of course, the longer the period of time over which drug will be released, all other parameters being kept equal. This is particularly so if the flake is bioerodable. The flakes also can be of different surface areas, which will affect the release kinetics of drugs contained therein or coated thereon. The plurality of flakes, therefore, can be a mixture of sizes, uniformly distributed over a range or be two or more discrete sizes to achieve a pulsed-type release, etc. The flakes can be relatively large so as to lend themselves to topical and oral delivery formats or can be extremely small, permitting them to be injected.

The morphology of the flakes also will affect the release profile of drugs from the flake. Smooth surfaces represent relatively smaller surface areas, whereas rough surfaces represent relatively larger surface areas, as is well known.

The materials from which the flakes are made also will affect the release profiles of drugs from the flakes. Again, this is well known to those of ordinary skill in this art. For example, a flake formed of melted and recrystallized drug and/or carrier will dissolve more slowly than a drug and/or carrier that simply are pressed into a flake without melting, due to the energy of the crystal lattice of the melted and recrystallized material. At one extreme, the flake can be made of a polymer or fiber that is not bioerodable, whereby the only drug released is that which diffuses from or is released by the flake as it passes through the gastrointestinal tract. At another extreme, the flake can be made of a material that erodes completely before it passes through the gastrointestinal tract. Such flakes can be made of materials which erode selectively in the stomach, materials which erode selectively in the small intestine, materials which erode selectively in the large intestine, or materials which will erode partially or completely in more than one of these selected tissue regions.

The flakes also can be made of ion exchange materials to cause a selective release of drugs in a particular tissue. One example is using a resin that will release a drug in the presence of high concentrations of sodium ions, such as are present in the small intestine. The flakes also can be manufactured from a mixture of monomers and drug, whereby the monomer is polymerized into a polymer about the drug to form a 'molecularly imprinted polymer', which acts as a cage for the drug molecule. Thus, the flakes may be made of biodegradable polymers and non-biodegradable polymers and non-polymers as is conventional, all selected to influence the release profile of drug.

One important class of polymers useful in the invention are the bioadhesive polymers. Such polymers can be fashioned as flakes containing drugs and will adhere to the intestine. This can accomplish a number of desirable results. First, it can increase residence time of the flakes in the intestine, thereby affecting the amount of drug released in the intestine. In addition, the

bioadhesive-containing drug will stick to the intestine, and act as a sustained-release delivery form for such time as it is present sticking to the intestine. The drug will be released slowly by diffusion or through degradation of the polymer in the intestine, thereby controlling the release profile of the drug.

The flakes also can be coated, applying principals conventional in the particle-based delivery art. Thus, the flakes can be coated with enteric coatings to permit the flakes to survive the environment of the stomach. The flakes can be coated with pH sensitive materials to cause the coating to dissolve only after the flake enters the intestine. Coatings which would dissolve at neutral pH, generally, are useful for this purpose. The flakes also can be coated with lipophilic coatings which tend to dissolve only after contacting the bile in the large intestine.

The thickness of such coatings, of course, also can be varied, whereby some flakes are exposed for drug delivery prior to others, thereby effecting an extended drug-release profile.

The coatings may be free of drug or may contain the drug. If the coating contains a drug, then it can be the same drug or a different drug than is in the flake. If it is the same drug, it can be of the same concentration or at a different concentration. Likewise, the coating can be made of the same material as the flake or of a different material than the flake. Thus, the flake can be a particular polymer containing a drug, and the coating can be the same polymer free of drug or the coating can be a different material altogether. It should be mentioned, as well, that the flake can contain a single drug or a combination of drugs.

The flakes also can be formed of a variety of layers, some of which can act as a coating. One layer can be a drug and another layer can be, inter alia, (1) a coating to influence the drug-release profile, (2) the same drug but at a different concentration, (3) a different drug, (4) a barrier layer to separate two layers, (5) a substrate for another layer, (6) a food, (7) a nonfood and so on. Thus, the flakes according to the invention may be 1, 2, 3, or more layers. Such layered flakes can be manufactured easily, such as, for example, by pressing two or more layers together, by spraying a plurality of layers sequentially onto a belt or drum, by vortexing preformed flakes to render them airborne in a mist that will coat the flakes to create another layer, and so on.

Flakes having any one or more of the foregoing characteristics can be manufactured by adapting existing technologies to flake manufacturing processes. For example, drugs can be incorporated into flakes at different concentrations by applying to two separate preparations of prefabricated porous flakes, drugs at different concentrations in solutions for diffusing into the two separate preparations of flakes. The flakes also can be made as molecular imprinted polymers,

whereby the polymer of the flake is made from the mixture of drug and monomer, with the drug being captured in the polymer formed from the monomer. Coatings of various thicknesses also can be applied as is conventional. Single, double, triple, and other multi-layered flakes, coated or not, thus can be formed. Mixtures of flakes with different characteristics also can be used, e.g. uncoated flakes with coated flakes, mixtures of flakes with different concentrations of drugs, mixtures of flakes with different thicknesses, mixtures of flakes carrying drugs with flakes that carry drug uptake enhances, etc.

According to one important embodiment, the sustained or controlled release microparticles of the prior art are used conventionally in the flake technology of the present invention. In this aspect of the invention, microparticles, such as microspheres and nanospheres, are incorporated into the flakes of the invention. In other words, microparticles first are formed having known and desired release-profiles characteristic of the prior art. Those microparticles then are formed as part of the flakes of the invention. The microparticles can be pressed into flakes, sprayed onto rotating drums as described in greater detail below and formed into flakes, covalently attached to flakes and the like. Thus, in order to achieve the release profiles characteristic of the prior art, no new technology is required. Instead, the flakes simply can act as a delivery vehicle for existing microparticles. Such a delivery vehicle would be particularly useful for oral preparations, topical preparations, and in other circumstances as will be apparent to those of ordinary skill in the art.

It has been mentioned that one important use of the flakes of the invention is for delivering drugs orally. Any drug which can be delivered orally according to the prior art can be delivered using the flake technology of the invention. Virtually any release profile obtained in the prior art using oral delivery formats also can be obtained using the flakes according to the invention. The flakes simply provide a convenient format for orally delivering drugs to particular target patient populations.

The flakes also can be used in topical formulations. The flakes will provide a smooth, non-gritty coating on the skin, which can be used for delivering topically drugs contained in or attached to the flakes. Such topical preparations include virtually all of the known drugs presently delivered topically, but never before delivered as part of a flake. In addition, the flakes are particularly suited for the delivery of certain agents, such as sunscreen agents and insecticides. For sunscreen agents, the flakes themselves could comprise a physical or chemical sunscreen agent, which could be used to form a protective barrier from the sun. Moreover, if the sunscreen agent is covalently attached to the flake, then the sunscreen agent can be prevented from entering cells,

thereby reducing or even eliminating any side effects for such sunscreen agents. The agent is held on the flake and is not released into the skin. The same benefit can be obtained when using flakes according to the invention to apply an insecticide. The insecticide can be covalently attached to the flakes which are topically applied as a smooth layer on the skin. Because the insecticides are covalently attached to the flakes, they are present for exerting the desired action, but they are not released generally in high dose into the skin, thereby avoiding potential unwanted side effects. Such sunscreen agents and insecticides on flakes also are desirable as the flakes themselves act as a smooth lubricant when applying the agents to the skin.

In topical preparations, the flakes, in general, are lubricating and therefore can prevent chafing of skin against skin or clothing against skin, as an additional benefit.

Flakes according to the invention also may be applied in preparations that are intended for body cavities, such as intravaginal preparations or suppository preparations. Agents such as antibiotics, antifungals, and the like can be attached to flakes and conveniently delivered. The feel of such flakes is superior to the feel of the microparticles of the prior art. Such topical preparations can include agents for treating genital warts, kaposi sarcoma, actinic keratosis and skin cancers in general.

The topical preparations of the invention also can be used for applying wound healing agents to the skin. The wound healing agents can be attached to, coated on, or contained within the flakes of the invention, which can be applied topically.

The flakes according to the invention also can be applied parenterally. The preparations of the invention are particularly suitable for local delivery of drug agents. The flakes of the invention have less mobility than microspheres when placed within the body, such as by injection into a solid tumor. Systemic exposure to the drug thereby is reduced and it is believed that a more consistent release profile is obtained. The flakes of the invention also can be used in a manner as described in the prior art by intravenous injection, whereby the flakes are manufactured at a particular size and become desirably lodged in capillaries.

Flakes according to the invention also can be used to cover areas in the body to prevent tissue adhesion, such as post-surgical tissue adhesion. The flakes can be made, for example, of hyaluronic acid, and applied to cover areas of tissue to prevent tissue adhesions.

The flakes of the invention thus can be included in any of the prior art forms used for administering drugs, including implants, topical preparations, inhalable preparations, suppositories, ocular formulations, oral formulations and the like, which are well known. In certain of the

preparations according to the invention, such as topical preparations, there may be included agents which are not suitable for oral ingestion. Such agents include creams, lubricants and the like which are well known.

The flakes according to the invention can be manufactured according to many well known methodologies. The flakes may be cast, such as by drum casting or bell casting. The flakes may be fractured, chipped or shaved from solid materials. The flakes may be pressed, stamped or embossed by conventional equipment. Likewise, the flakes may be milled such as using a roller milling apparatus. The flakes also may be extruded such as in the form of a ribbon which is broken into smaller pieces. The flakes also may be rolled from wet particulates. Exemplary materials for making flakes include polyvinyl alcohol, poly(vinylpyrollidone), methyl cellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, agar, carrageenan, xanthan, polyethylene glycol, a copolymer of acrylic and methacrylic acid esters, ethylcellulose, cellulose acetate, cellulose acetate phthalate, poly(methyl methacrylate), poly(methyl acrylate), polyethylene, polypropylene, polyethylene oxide, PET, poly(vinyl isobutyl ether), poly(vinyl acetate), poly(vinyl chloride), polyurethane, pectin, furcellaran, starch, zein, gelatin, collagen, polygeline, alginic acid, propylene glycol alginate or sodium alginate.

A more comprehensive list is materials including, but not limited to, nonbioerodable and bioerodable polymers. Such polymers have been described in great detail in the prior art. They include, but are not limited to: polyamides, polycarbonates, polyalkylenes, polyalkylene glycols, polyalkylene oxides, polyalkylene terepthalates, polyvinyl alcohols, polyvinyl ethers, polyvinyl esters, polyvinyl halides, polyvinylpyrrolidone, polyglycolides, polysiloxanes, polyurethanes and copolymers thereof, alkyl cellulose, hydroxyalkyl celluloses, cellulose ethers, cellulose esters, nitro celluloses, polymers of acrylic and methacrylic esters, methyl cellulose, ethyl cellulose, hydroxypropyl cellulose, hydroxy-propyl methyl cellulose, hydroxybutyl methyl cellulose, cellulose acetate, cellulose propionate, cellulose acetate butyrate, cellulose acetate phthalate, carboxylethyl cellulose, cellulose triacetate, cellulose sulphate sodium salt, poly (methyl methacrylate), poly(ethylmethacrylate), poly(butylmethacrylate), poly(isobutylmethacrylate), poly(hexlmethacrylate), poly(isodecylmethacrylate), poly(lauryl methacrylate), poly (phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecyl acrylate), polyethylene, polypropylene poly(ethylene glycol), poly(ethylene oxide), poly(ethylene terephthalate), poly(vinyl alcohols), poly(vinyl acetate, poly vinyl chloride polystyrene and polyvinylpryrrolidone.

Examples of preferred non-biodegradable polymers include ethylene vinyl acetate, poly(meth) acrylic acid, polyamides, copolymers and mixtures thereof.

Examples of preferred biodegradable polymers include synthetic polymers such as polymers of lactic acid and glycolic acid, polyanhydrides, poly(ortho)esters, polyurethanes, poly(butic acid), poly(valeric acid), poly(caprolactone), poly(hydroxybutyrate), poly(lactide-co-glycolide) and poly(lactide-co-caprolactone), and natural polymers such as alginate and other polysaccharides that include but are not limited to arabinans, fructans, fucans, galactans, galacturonans, glucans, mannans, xylans (such as, for example, inulin), levan, fucoidan, carrageenan, galatocarolose, pectic acid, pectin, amylose, pullulan, glycogen, amylopectin, cellulose, dextran, pustulan, chitin, agarose, keratan, chondroitan, dermatan, hyaluronic acid, alginic acid, xanthan gum, starch and various other natural homopolymer or heteropolymers such as those containing one or more of the following aldoses, ketoses, acids or amines: erythrose, threose, ribose, arabinose, xylose, lyxose, allose, altrose, glucose, mannose, gulose, idose, galactose, talose, erythrulose, ribulose, xylulose, psicose, fructose, sorbose, tagatose, mannitol, sorbitol, lactose, sucrose, trehalose, maltose, cellobiose, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, histidine, glucuronic acid, gluconic acid, glucaric acid, galacturonic acid, mannuronic acid, glucosamine, galactosamine, and neuraminic acid, and naturally occurring derivatives thereof, and including dextran and cellulose, collagen, chemical derivatives thereof (substitutions, additions of chemical groups, for example, alkyl, alkylene, hydroxylations, oxidations, and other modifications routinely made by those skilled in the art), albumin and other hydrophilic proteins, zein and other prolamines and hydrophobic proteins, copolymers and mixtures thereof. In general, these materials degrade either by enzymatic hydrolysis or exposure to water *in vivo*, by surface or bulk erosion. The foregoing materials may be used alone, as physical mixtures (blends), or as co-polymers. The most preferred polymers are polyesters, polyanhydrides, polystyrenes and blends thereof.

Particularly preferred in some embodiments are bioadhesive polymers. A bioadhesive polymer is one that binds to mucosal epithelium under normal physiological conditions. Bioadhesion in the gastrointestinal tract proceeds in two stages: (1) viscoelastic deformation at the point of contact of the synthetic material into the mucus substrate, and (2) formation of bonds between the adhesive synthetic material and the mucus or the epithelial cells. In general, adhesion of polymers to tissues may be achieved by (i) physical or mechanical bonds, (ii) primary or covalent chemical bonds, and/or (iii) secondary chemical bonds (i.e., ionic). Physical or mechanical bonds can result from deposition and inclusion of the adhesive material in the crevices of the mucus or the

folds of the mucosa. Secondary chemical bonds, contributing to bioadhesive properties, consist of dispersive interactions (i.e., Van der Waals interactions) and stronger specific interactions, which include hydrogen bonds. The hydrophilic functional groups primarily responsible for forming hydrogen bonds are the hydroxyl and the carboxylic groups. Numerous bioadhesive polymers are discussed in that application. Representative bioadhesive polymers of particular interest include biocrodible hydrogels described by H.S. Sawhney, C.P. Pathak and J.A. Hubell in Macromolecules, 1993, 26:581-587, the teachings of which are incorporated herein, polyhyaluronic acids, casein, gelatin, glutin, polyanhydrides, polyacrylic acid, alginate, chitosan, poly(methyl methacrylates), poly(ethyl methacrylates), poly butylmethacrylate), poly(isobutylmethacrylate), poly(hexlmethacrylate), poly(isodecl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly (methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), and poly(octadecl acrylate). Most preferred is poly(fumaric-co-sebacic)acid. Other suitable bioadhesives are pectin, a mixture of sulfated sucrose and aluminum hydroxide, hydrophilic polysaccharide gums such as natural plant exudates, including karaya gum, ghatti gum, tragacanth gum, xanthan gum, jaraya gum and the like, as well as seed gums such as guar gum, locust bean gum, psillium seed gum and the like.

Polymers with enhanced bioadhesive properties can be provided wherein anhydride monomers or oligomers are incorporated into the polymer. The oligomer excipients can be blended or incorporated into a wide range of hydrophilic and hydrophobic polymers including proteins, polysaccharides and synthetic biocompatible polymers. Anhydride oligomers may be combined with metal oxide particles to improve bioadhesion even more than with the organic additives alone. Organic dyes because of their electronic charge and hydrophobicity/ hydrophilicity can either increase or decrease the bioadhesive properties of polymers when incorporated into the polymers. The incorporation of oligomer compounds into a wide range of different polymers which are not normally bioadhesive dramatically increases their adherence to tissue surfaces such as mucosal membranes.

As used herein, the term "anhydride oligomer" refers to a diacid or polydiacids linked by anhydride bonds, and having carboxy end groups linked to a monoacid such as acetic acid by anhydride bonds. The anhydride oligomers have a molecular weight less than about 5000, typically between about 100 and 5000 daltons, or are defined as including between one to about 20 diacid units linked by anhydride bonds. In one embodiment, the diacids are those normally found in the Krebs glycolysis cycle. The anhydride oligomer compounds have high chemical reactivity.

The oligomers can be formed in a reflux reaction of the diacid with excess acetic anhydride. The excess acetic anhydride is evaporated under vacuum, and the resulting oligomer, which is a mixture of species which include between about one to twenty diacid units linked by anhydride bonds, is purified by recrystallizing, for example from toluene or other organic solvents. The oligomer is collected by filtration, and washed, for example, in ethers. The reaction produces anhydride oligomers of mono and poly acids with terminal carboxylic acid groups linked to each other by anhydride linkages.

The anhydride oligomer is hydrolytically labile. As analyzed by gel permeation chromatography, the molecular weight may be, for example, on the order of 200-400 for fumaric acid oligomer (FAPP) and 2000-4000 for sebacic acid oligomer (SAPP). The anhydride bonds can be detected by Fourier transform infrared spectroscopy by the characteristic double peak at 1750 cm^{-1} and 1820 cm^{-1}, with a corresponding disappearance of the carboxylic acid peak normally at 1700 cm^{-1}.

In one embodiment, the oligomers may be made from diacids described for example in U.S. Patent No. 4,757,128 to Domb et al., U.S. Patent No. 4,997,904 to Domb, and U.S. Patent No. 5,175,235 to Domb et al., the disclosures of which are incorporated herein by reference. For example, monomers such as sebacic acid, bis(p-carboxy-phenoxy)propane, isophathalic acid, fumaric acid, maleic acid, adipic acid or dodecanedioic acid may be used.

Organic dyes, because of their electronic charge and hydrophilicity/hydrophobicity, may alter the bioadhesive properties of a variety of polymers when incorporated into the polymer matrix or bound to the surface of the polymer. A partial listing of dyes that affect bioadhesive properties include, but are not limited to: acid fuchsin, alcian blue, alizarin red s, auramine o, azure a and b, Bismarck brown y, brilliant cresyl blue ald, brilliant green, carmine, cibacron blue 3GA, congo red, cresyl violet acetate, crystal violet, cosin b, eosin y, erythrosin b, fast green fcf, giemsa, hematoylin, indigo carmine, Janus green b, Jenner's stain, malachite green oxalate, methyl blue, methylene blue, methyl green, methyl violet 2b, neutral red, Nile blue a, orange II, orange G, orcein, paraosaniline chloride, phloxine b, pyronin b and y, reactive blue 4 and 72, reactive brown 10, reactive green 5 and 19, reactive red 120, reactive yellow 2,3, 13 and 86, rose bengal, safranin o, Sudan III and IV, Sudan black B and toluidine blue.

Fatty acids are carboxylic acid compounds found in animal and vegetable fat and oil. Fatty acids are classified as lipids and are composed of chains of alkyl groups containing from 4 to 22 carbon atoms and 0-3 double bonds and characterized by a terminal carboxyl group, -COOH. Fatty

acids may be saturated or unsaturated and may be solid, semisolid, or liquid. The most common saturated fatty acids are butyric acid (C4), lauric acid (C12), palmitic acid (C16), and stearic acid (C18). Unsaturated fatty acids are usually derived from vegetables and consist of alkyl chains containing from 16 to 22 carbon atoms and 0-3 double bonds with the characteristic terminal carboxyl group. The most common unsaturated fatty acids are oleic acid, linoleic acid, and linolenic acid (all C18 acids).

Simple lipids can be esters of fatty acids, triglycerides, cholesterol esters and vitamin A and D esters. Compound lipids can be phospholipids, glycolipids (cerebrosides), sulfolipids, lipoproteins and lipopolysaccharides. Derived lipids can be saturated and unsaturated fatty acids and mono or diglycerides. Analogs of these lipids can also be used.

Examples of lipids are: triglycerides-triolein, fatty acids-linoleic, linolenic and arachidonic; sterols -testosterone, progesterone, cholesterol; phospholipids-phosphatidic acid, lecithin, cephalin (phosphatidyl ethanolamine) sphingomyleins; glycolipids -cerebosides, gangliosides.

The lipids used may be of either natural, synthetic or semi-synthetic origin.

Lipids which may be used to prepare the flakes used in the present invention include but are not limited to: lipids such as fatty acids, lysolipids, phosphatidylcholine with both saturated and unsaturated lipids including dioleoylphosphatidylcholine; dimyristoylphosphatidylcholine; dipentadecanoylphosphatidylcholine; dilauroylphosphatidylcholine; dipalmitoylphosphatidylcholine (DPPC); distearoylphosphatidylcholine (DSPC); phosphatidylethanolamines such as dioleoylphosphatidylethanolamine and dipalmitoylphosphatidylethanolamine (DPPE); phosphatidylserine; phosphatidylglycerol; phosphatidylinositol; sphingolipids such as sphingomyelin; glycolipids such as ganglioside GM1 and GM2; glucolipids; sulfatides; glycosphingolipids; phosphatidic acids such as dipalymitoylphosphatidic acid (DPPA); palmitic acid; stearic acid; arachidonic acid; oleic acid; lipids bearing polymers such as polyethyleneglycol, i.e., PEGylated lipids, chitin, hyaluronic acid or polyvinylpyrrolidone; lipids bearing sulfonated mono-, di-, oligo- or polysaccharides; cholesterol, cholesterol sulfate and cholesterol hemisuccinate; tocopherol hemisuccinate; lipids with ether and ester-linked fatty acids; polymerized lipids (a wide variety of which are well known in the art); diacetyl phosphate; dicetyl phosphate; stearylamine; cardiolipin; phospholipids with short chain fatty acids of 6-8 carbons in length; synthetic phospholipids with asymmetric acyl chains (e.g., with one acyl chain of 6 carbons and another acyl chain of 12 carbons); ceramides; non-ionic liposomes including niosomes such as polyoxyethylene fatty acid esters, polyoxyethylene fatty alcohols, polyoxyethylene fatty alcohol ethers,

polyoxyethylated sorbitan fatty acid esters, glycerol polyethylene glycol oxystearate, glycerol polyethylene glycol ricinoleate, ethoxylated soybean sterols, ethoxylated castor oil, polyoxyethylene- polyoxypropylene polymers, and polyoxyethylene fatty acid stearates; sterol aliphatic acid esters including cholesterol sulfate, cholesterol butyrate, cholesterol iso-butyrate, cholesterol palmitate, cholesterol stearate, lanosterol acetate, ergosterol palmitate, and phytosterol n-butyrate; sterol esters of sugar acids including cholesterol glucuronide, lanosterol glucuronide, 7-dehydrocholesterol glucuronide, ergosterol glucuronide, cholesterol gluconate, lanosterol gluconate, and ergosterol gluconate; esters of sugar acids and alcohols including lauryl glucuronide, stearoyl glucuronide, myristoyl glucuronide, lauryl gluconate, myristoyl gluconate, and stearoyl gluconate; esters of sugars and aliphatic acids including sucrose laurate, fructose laurate, sucrose palmitate, sucrose stearate, glucuronic acid, gluconic acid, accharic acid, and polyuronic acid; saponins including sarsasapogenin, smilagenin, hederagenin, oleanolic acid, and digitoxigenin; glycerol dilaurate, glycerol trilaurate, glycerol dipalmitate, glycerol and glycerol esters including glycerol tripalmitate, glycerol distearate, glycerol tristearate, glycerol dimyristate, glycerol trimyristate; longchain alcohols including n-decyl alcohol, lauryl alcohol, myristyl alcohol, cetyl alcohol, and n-octadecyl alcohol; 6-(5-cholesten-3 beta -yloxy)-1 -thio- beta -D-galactopyranoside; digalactosyldiglyceride; 6-(5-cholesten-3 beta -yloxy)hexyl-6-amino-6-deoxy-1-thio- beta -D-galactopyranoside; 6-(5-cholesten-3 beta -yloxy)hexyl-6-amino-6-deoxyl-1-thio- alpha -D-mannopyranoside; 12-(((7'-diethylaminocoumarin-3-yl)carbonyl)methylamino)-octadecanoic acid; N-[12-(((7'-diethylaminocoumarin-3-yl)carbonyl)methyl-amino) octadecanoyl]-2-aminopalmitic acid; cholesteryl)4'-trimethylammonio)butanoate; N-succinyldioleoylphosphatidylethanolamine; 1,2-dioleoyl-sn-glycerol;1,2-dipalmitoyl-sn-3-succinylglycerol; 1,3-dipalmitoyl-2-succinylglycerol; 1-hexadecyl-2-palmitoyl- glycerophosphoethanolamine and palmitoylhomocysteine, and/or combinations thereof.

If desired, a variety of cationic lipids such as DOTMA, N-[1-(2,3-diolcoyloxy)propyl] -N,N,N-trimethylammoium chloride; DOTAP, 1,2-diolcoyloxy-3-(trimethylammonio)propane; and DOTB, 1,2-dioleoyl-3-(4'-trimethyl-ammonio)butanoyl-sn-glycerol may be used. In general the molar ratio of cationic lipid to non-cationic lipid in the liposome may be, for example, 1:1000, 1:100, preferably, between 2:1 to 1:10, more preferably in the range between 1:1 to 1:2.5 and most preferably 1:1 (ratio of mole amount cationic lipid to mole amount non-cationic lipid, e.g., DPPC). A wide variety of lipids may comprise the non-cationic lipid when cationic lipid is used to construct

the microsphere. Preferably, this non-cationic lipid is dipalmitoylphosphatidylcholine, dipalmitoylphosphatidylethanolamine or dioleoylphosphatidylethanolamine. In lieu of cationic lipids as described above, lipids bearing cationic polymers such as polylysine or polyarginine, as well as alkyl phosphonates, alkyl phosphinates, and alkyl phosphites, may also be used to construct the flakes.

In addition, examples of saturated and unsaturated fatty acids that may be used to prepare the flakes used in the present invention, may include molecules that may contain preferably between 12 carbon atoms and 22 carbon atoms in either linear or branched form. Hydrocarbon groups consisting of isoprenoid units and/or prenyl groups can be used as well. Examples of saturated fatty acids that are suitable include, but are not limited to, lauric, myristic, palmitic, and stearic acids; examples of unsaturated fatty acids that may be used are, but are not limited to, lauroleic, physeteric, myristoleic, palmitoleic, petroselinic, and oleic acids; examples of branched fatty acids that may be used are, but are not limited to, isolauric, isomyristic, isopalmitic, and isostearic acids. In addition, to the saturated and unsaturated groups, gas and gaseous precursor filled mixed micelles can also be composed of 5 carbon isoprenoid and prenyl groups.

Waxes can also be used to form the flakes of the invention. In general, waxes are long chain fatty alcohol esters of fatty acids. Many waxes have suitable melting characteristics for use in the compositions of the invention, since they are solids at 25 °C. Examples include animal waxes, vegetable waxes, petroleum waxes, synthetic waxes, and mixtures thereof and include without limitation beeswax, lanolin, candelilla wax, carnauba wax, microcrystalline wax, carbowax, and mixtures thereof. Preferred waxes are made from saturated or monounsaturated fatty acids and saturated or unsaturated fatty alcohols. An example of the latter is provided by arachidyl oleate.

Suitable enteric coatings for flakes include ethylcellulose, polyvinylchloride, methylcellulose, polyurethane, cellulose acetate, polycarbonate, polyethylene, polypropylene, shellac and polymers of acrylic and methyl acrylic acids and esters of it.

In another embodiment of the invention, the drug-incorporated flakes may be incorporated into a semi-solid base to form a spoon-able drug delivery system. The semi-solid base may be comprised of pectin, guar gum, xanthan gum, gum arabic, gum acacia, locust bean gum, carageenan gum, alginic acid, psyllium hydrocolloid, oat bran gum, rice bran gum, glucomannan, traganth gum, karaya gum, tapioca, corn starch, cellulose gums, agar, gelatin, polyacrylates, polysaccharides, polyvinylpyrolidones, pyrrolidones, polyols, collagen, polyethylene glycols, polyvinylalcohols, polyethers, polyesters, natural or synthetic oils, liquid paraffin, beeswax, silicon waves, natural or

modified fatty acids, or combinations of thereof. Additionally viscous fruit purees such as apple, prune, apricot, pear, pineapple, banana, grape, strawberry, raspberry, blackberry, boysenberry, loganberry, dewberry, gooseberry, cranberry, mulberry, elderberry, blueberry, fig, currant, kiwi may be used.

In a preferred embodiment, the drug-incorporated flakes may be incorporated into the nutritionally fortified delivery vehicle (NFDV) of the invention to form a spoon-able drug delivery system with additional advantages of providing needed dietary requirements. See below for a more detailed discussion of the NFDV.

Nutritionally Fortified Delivery Vehicle (NFDV)

A spoon-feedable base specially fortified to enhance therapeutic effect is developed. The base could be either modeled after a dietary supplement currently formulated and administered in numerous extended health care facilities throughout the country or developed specifically to enhance the drug uptake.

The NFDV could be administered as a freestanding product as well as in combination with drugs. The NFDV will be formulated to consist of a viscosity that will facilitate spoon administration to patients currently unable to swallow tables, capsules, or liquid dosage forms.

The NFDV could complement the drug uptake. It has been demonstrated by Dr. Wurtman certain carbohydrate-to-protein ratios enhance the effect of dopamine. Thus, the NFDV may be formulated to enhance certain desired effects of the administered drugs.

The NFDV could also complement other dietary issues, for example, addressing complications associated with the administration of narcotics. The uptake of narcotics, such as morphine, causes the inability to produce bowel movement. Also, many patients under morphine treatment cannot swallow solid food. Incorporation the morphine into fortified high fiber base wil allow an easy spoon-fed administration of the drug and the ability to enhance bowel movement with dietary fiber.

The high occurrence of constiption in the elderly population has necessitated the addition of high fiber as a dietary supplement. Such a base is also suited for elderly patients who need the supplement fiber for regular bowel movement (10 g a day). The NFDV may also contain simethicone to reduce flatulation.

Table 1 describes some modifications for NFDV compositions designed to compliment treatment of a particular disease state.

Table 1. Benefits of particular NFDV composition as a complimentary to a drug to treat a particular disease state (Adapted from Windhover Information, Inc. pp. 14, 1997)

Disease State	NFDV Composition
Renal failure	different proteins
Liver disease	different proteins
Hypermetabolic States	different proteins, amino acids and vitamins
Lung disease	High fat, low carbohydrate
HIV	enriched with specific amino acids and vitamins
Diabetes mellitus	carbohydrates, high fiber
Mal-absorption	specific fats

The NFDV could be fortified with vitamins (C, D, E), flavorings (citric acid, ascorbic acid, menthol, sorbitol, xylitol).

Container

An oral medication delivery system, wherein said container means comprises a dual or multiple chamber container. The container could be a rigid substantially cylindrical tube and said container means includes rupturable membrane means for separating the container into first and second chambers, wherein said pharmaceutically active agent in powder form is disposed within said first chamber and the NFDV is disposed within said second chamber, removable seal means for sealing said delivery liquid in said second chamber, and plunger means for sealing said pharmaceutically active agent in said first chamber and for rupturing said rupturable membrane to mix said pharmaceutically active agent and said delivery liquid.

While the above examples have addressed the needs of the geriatric population, it will be readily apparent that the invention may be applied to other populations which experience difficulty in taking conventional solid and liquid dosage formats. For example, pediatric, oncology or other patients who cannot swallow will benefit from a spoon-able drug delivery dosage form (SADD). Similarly to the elderly, young children cannot handle the swallowing of a tablet and prefer a dosage form that could be spoon-fed to them. Cancer patients who undergo radiation therapy of the head and neck area or take chemotheraputic drugs experience the lack of formation of saliva and/or esaphogatis which results in inability to take solid food such as tablets.

Examples of drugs that might be utilized in a delivery application of the invention include literally any hydrophilic or hydrophobic drug at a concentration for having a therapeutic benefit. Preferably, though not necessarily, the drug is one that has already been deemed safe and effective for use by the appropriate governmental agency or body. For example, drugs for human use listed

by the FDA under 21 C.F.R. 330.5, 331 through 361; 440-460; drugs for veterinary use listed by the FDA under 21 C.F.R. 550-582, incorporated herein by reference, are all considered acceptable for use in the present novel polymer networks.

The term "drug" includes pharmacologically active substances that produce a local or systemic therapeutic effect in animals, plants, or viruses. The term thus means any substance intended for use in the diagnosis, or therapeutic treatment or prevention of disease. The term "animal" used herein is taken to mean mammals, such as primates, including humans, sheep, horses, cattle, pigs, dogs, cats, rats, mice, birds, reptiles, fish, insects, arachnids, protists (e.g. protozoa), and prokaryotic bacteria. The term "plant" means higher plants (angiosperms, gymnosperms), fungi, and prokaryotic blue-green "algae" (i.e. cyanobacteria).

The drug can be any type of compound including proteins, polypeptides, polynucleotides, nucleoproteins, polysaccharieds, glycoproteins, lipoproteins, and synthetic and biologically engineered analogs thereof. The term "protein" is art-recognized and for purposes of this invention also encompasses peptides. The proteins or peptides may be any biologically active protein or peptide, naturally occurring or synthetic.

Examples of proteins include antibodies, enzymes, steroids, growth hormone and growth hormone-releasing hormone, gonadotropin-releasing hormone, and its agonist and antagonist analogues, somatostatin and its analogues, gonadotropins such as luteinizing hormone and follicle-stimulating hormone, peptide-T, thyrocalcitonin, parathyroid hormone, glucagon, vasopressin, oxytocin, angiotensin I and II, bradykinin, kallidin, adrenocorticotropic hormone, thyroid stimulating hormone, insulin, glucagon and the numerous analogues and congeners of the foregoing molecules.

In general, the agents which can be delivered in the flakes of the invention, include, but are not limited to, adhesives, gases, pesticides, herbicides, fragrances, antifoulants, dies, salts, oils, inks, catalysts, detergents, curing agents, flavors, foods, fuels, metals, paints, photographic agents, biocides, pigments, plasticizers, propellants and the like.

The agent also may be a drug. A drug is to be distinguished from a food neutraceutical. Drug, as used herein, is meant to exlude nontherapeutic amounts of vitamins and minerals. Drugs, as used herein, also specifically exeludes foods. Flakes are known in the prior art as food, such as oatmeal flakes and grape-nut flakes. Often these foods are fortified with non-therapeutic amounts of vitamins, minerals and the like. The present definition of drug is specifically intended to exclude such prior art foods and fortified foods. The present invention, instead, involves the delivery of drugs for therapeutic treatment of disease states. The drug can be, but is not limited to:adrenergic

agent; adrenocortical steroid; adrenocortical suppressant; aldosterone antagonist; amino acid; anabolic; analeptic; analgesic; anesthetic; anorectic; anti-acne agent; anti-adrenergic; anti-allergic; anti-amebic; anti-anemic; anti-anginal; anti-arthritic; anti-asthmatic; anti-atherosclerotic; antibacterial; anticholinergic; anticoagulant; anticonvulsant; antidepressant; antidiabetic; antidiarrheal; antidiuretic; anti-emetic; anti-epileptic; antifibrinolytic; antifungal; antihemorrhagic; antihistamine; antihyperlipidemia; antihypertensive; antihypotensive; anti-infective; anti-inflammatory; antimicrobial; antimigraine; antimitotic; antimycotic, antinauseant, antineoplastic, antineutropenic, antiparasitic; antiproliferative; antipsychotic; antirheumatic; antiseborrheic; antisecretory; antispasmodic; antithrombotic; anti-ulcerative; antiviral; appetite suppressant; blood glucose regulator; bone resorption inhibitor; bronchodilator; cardiovascular agent; cholinergic; depressant; diagnostic aid; diuretic; dopaminergic agent; estrogen receptor agonist; fibrinolytic; fluorescent agent; free oxygen radical scavenger; gastric acid supressant; gastrointestinal motility effector; glucocorticoid; hair growth stimulant; hemostatic; histamine H2 receptor antagonists; hormone; hypocholesterolemic; hypoglycemic; hypolipidemic; hypotensive; imaging agent; immunizing agent; immunomodulator; immunoregulator; immunostimulant; immunosuppressant; keratolytic; LHRH agonist; mood regulator; mucolytic; mydriatic; nasal decongestant; neuromuscular blocking agent; neuroprotective; NMDA antagonist; non-hormonal sterol derivative; plasminogen activator; platelet activating factor antagonist; platelet aggregation inhibitor; psychotropic; radioactive agent; scabicide; sclerosing agent; sedative; sedative-hypnotic; selective adenosine Al antagonist; serotonin antagonist; serotonin inhibitor; serotonin receptor antagonist; steroid; thyroid hormone; thyroid inhibitor; thyromimetic; tranquilizer; amyotrophic lateral sclerosis agent; cerebral ischemia agent; Paget's disease agent; unstable angina agent; vasoconstrictor; vasodilator; wound healing agent; xanthine oxidase inhibitor.

Examples include:

Adrenergic: Adrenalone; Amidephrine Mesylate; Apraclonidine Hydrochloride; Brimonidine Tartrate; Dapiprazole Hydrochloride; Deterenol Hydrochloride; Dipivefrin; Dopamine Hydrochloride; Ephedrine Sulfate; Epinephrine; Epinephrine Bitartrate; Epinephryl Borate; Esproquin Hydrochloride; Etafedrine Hydrochloride; Hydroxyamphetamine Hydrobromide; Levonordefrin; Mephentermine Sulfate; Metaraminol Bitartrate; Metizoline Hydrochloride; Naphazoline Hydrochloride; Norepinephrine Bitartrate; Oxidopamine; Oxymetazoline Hydrochloride; Phenylephrine Hydrochloride; Phenylpropanolamine Hydrochloride; Phenylpropanolamine Polistirex; Prenalterol Hydrochloride; Propylhexedrine; Pseudoephedrine

Hydrochloride; Tetrahydrozoline Hydrochloride; Tramazoline Hydrochloride; Xylometazoline Hydrochloride.

Adrenocortical steroid: Ciprocinonide; Desoxycorticosterone Acetate; Desoxycorticosterone Pivalate; Dexamethasone Acetate; Fludrocortisone Acetate; Flumoxonide; Hydrocortisone Hemisuccinate; Methylprednisolone Hemisuccinate; Naflocort; Procinonide; Timobesone Acetate; Tipredane.

Adrenocortical suppressant: Aminoglutethimide; Trilostane.

Alcohol deterrent: Disulfiram.

Aldosterone antagonist: Canrenoate Potassium; Canrenone; Dicirenone; Mexrenoate Potassium; Prorenoate Potassium; Spironolactone.

Amino acid: Alanine; Aspartic Acid; Cysteine Hydrochloride; Cystine; Histidine; Isoleucine; Leucine; Lysine; Lysine Acetate; Lysine Hydrochloride; Methionine; Phenylalanine; Proline; Serine; Threonine; Tryptophan; Tyrosine; Valine.

Ammonia detoxicant: Arginine; Arginine Glutamate; Arginine Hydrochloride.

Anabolic: Bolandiol Dipropionate; Bolasterone; Boldenone Undecylenate; Bolenol; Bolmantalate; Ethylestrenol; Methenolone Acetate; Methenolone Enanthate; Mibolerone; Nandrolone Cyclotate; Norbolethone; Pizotyline; Quinbolone; Stenbolone Acetate; Tibolone; Zeranol.

Analeptic: Modafinil.

Analgesic: Acetaminophen; Alfentanil Hydrochloride; Aminobenzoate Potassium; Aminobenzoate Sodium; Anidoxime; Anileridine; Anileridine Hydrochloride; Anilopam Hydrochloride; Anirolac; Antipyrine; Aspirin; Benoxaprofen; Benzydamine Hydrochloride; Bicifadine Hydrochloride; Brifentanil Hydrochloride; Bromadoline Maleate; Bromfenac Sodium; Buprenorphine Hydrochloride; Butacetin; Butixirate; Butorphanol; Butorphanol Tartrate; Carbamazepine;

Carbaspirin Calcium; Carbiphene Hydrochloride; Carfentanil Citrate; Ciprefadol Succinate; Ciramadol; Ciramadol Hydrochloride; Clonixeril; Clonixin; Codeine ; Codeine Phosphate; Codeine Sulfate; Conorphone Hydrochloride; Cyclazocine; Dexoxadrol Hydrochloride; Dexpemedolac; Dezocine; Diflunisal; Dihydrocodeine Bitartrate; Dimefadane; Dipyrone; Doxpicomine Hydrochloride; Drinidene; Enadoline Hydrochloride; Epirizole; Ergotamine Tartrate; Ethoxazene Hydrochloride; Etofenamate; Eugenol; Fenoprofen; Fenoprofen Calcium; Fentanyl Citrate; Floctafenine; Flufenisal; Flunixin; Flunixin Meglumine; Flupirtine Maleate; Fluproquazone; Fluradoline Hydrochloride; Flurbiprofen ; Hydromorphone Hydrochloride; Ibufenac; Indoprofen; Ketazocine; Ketorfanol; Ketorolac Tromethamine; Letimide Hydrochloride; Levomethadyl Acetate; Levomethadyl Acetate Hydrochloride; Levonantradol Hydrochloride; Levorphanol Tartrate; Lofemizole Hydrochloride; Lofentanil Oxalate; Lorcinadol; Lornoxicam; Magnesium Salicylate; Mefenamic Acid; Menabitan Hydrochloride; Meperidine Hydrochloride; Meptazinol Hydrochloride; Methadone Hydrochloride; Methadyl Acetate; Methopholine; Methotrimeprazine; Metkephamid Acetate; Mimbane Hydrochloride; Mirfentanil Hydrochloride; Molinazone; Morphine Sulfate; Moxazocine; Nabitan Hydrochloride; Nalbuphine Hydrochloride; Nalmexone Hydrochloride ; Namoxyrate; Nantradol Hydrochloride; Naproxen ; Naproxen Sodium ; Naproxol; Nefopam Hydrochloride; Nexeridine Hydrochloride; Noracymethadol Hydrochloride; Ocfentanil Hydrochloride; Octazamide; Olvanil; Oxetorone Fumarate; Oxycodone; Oxycodone Hydrochloride; Oxycodone Terephthalate; Oxymorphone Hydrochloride; Pemedolac; Pentamorphone; Pentazocine; Pentazocine Hydrochloride; Pentazocine Lactate; Phenazopyridine Hydrochloride; Phenyramidol Hydrochloride; Picenadol Hydrochloride; Pinadoline; Pirfenidone; Piroxicam Olamine; Pravadoline Maleate; Prodilidine Hydrochloride; Profadol Hydrochloride; Propiram Fumarate; Propoxyphene Hydrochloride; Propoxyphene Napsylate; Proxazole ; Proxazole Citrate ; Proxorphan Tartrate; Pyrroliphene Hydrochloride; Remifentanil Hydrochloride; Salcolex ; Salethamide Maleate; Salicylamide; Salicylate Meglumine; Salsalate ; Sodium Salicylate; Spiradoline Mesylate; Sufentanil; Sufentanil Citrate; Talmetacin ; Talniflumate ; Talosalate ; Tazadolene Succinate; Tebufelone ; Tetrydamine ; Tifurac Sodium; Tilidine Hydrochloride; Tiopinac; Tonazocine Mesylate; Tramadol Hydrochloride; Trefentanil Hydrochloride; Trolamine; Veradoline Hydrochloride; Verilopam Hydrochloride; Volazocine; Xorphanol Mesylate; Xylazine Hydrochloride; Zenazocine Mesylate; Zomepirac Sodium ; Zucapsaicin.

Androgen: Fluoxymesterone; Mesterolone; Methyltestosterone; Nandrolone Decanoate; Nandrolone Phenpropionate; Nisterime Acetate; Oxandrolone; Oxymetholone; Silandrone; Stanozolol; Testosterone; Testosterone Cypionate; Testosterone Enanthate; Testosterone Ketolaurate; Testosterone Phenylacetate; Testosterone Propionate; Trestolone Acetate.

Anesthesia, adjunct to: Sodium Oxybate.

Anesthetic: Aliflurane; Benoxinate Hydrochloride; Benzocaine; Biphenamine Hydrochloride ; Bupivacaine Hydrochloride; Butamben; Butamben Picrate; Chloroprocaine Hydrochloride; Cocaine; Cocaine Hydrochloride; Cyclopropane; Desflurane; Dexivacaine; Diamocaine Cyclamate; Dibucaine; Dibucaine Hydrochloride; Dyclonine Hydrochloride; Enflurane; Ether; Ethyl Chloride; Etidocaine; Etoxadrol Hydrochloride; Euprocin Hydrochloride; Fluroxene; Halothane; Isobutamben; Isoflurane; Ketamine Hydrochloride; Levoxadrol Hydrochloride ; Lidocaine; Lidocaine Hydrochloride; Mepivacaine Hydrochloride; Methohexital Sodium; Methoxyflurane; Midazolam Hydrochloride; Midazolam Maleate; Minaxolone; Nitrous Oxide; Norflurane; Octodrine; Oxethazaine; Phencyclidine Hydrochloride; Pramoxine Hydrochloride; Prilocaine Hydrochloride; Procaine Hydrochloride; Propanidid; Proparacaine Hydrochloride; Propofol; Propoxycaine Hydrochloride; Pyrrocaine; Risocaine; Rodocaine; Roflurane; Salicyl Alcohol; Sevoflurane; Teflurane; Tetracaine; Tetracaine Hydrochloride; Thiamylal; Thiamylal Sodium; Thiopental Sodium ; Tiletamine Hydrochloride; Zolamine Hydrochloride.

Anorectic compounds including dexfenfluramine.

Anorexic: Aminorex; Amphecloral; Chlorphentermine Hydrochloride; Clominorex; Clortermine Hydrochloride; Diethylpropion Hydrochloride; Fenfluramine Hydrochloride; Fenisorex; Fludorex; Fluminorex; Levamfetamine Succinate; Mazindol; Mefenorex Hydrochloride; Phenmetrazine Hydrochloride; Phenterminc; Sibutramine Hydrochloride.

Antagonist: Atipamezole; Atosiban; Bosentan; Cimetidine; Cimetidine Hydrochloride; Clentiazem Maleate; Detirelix Acetate; Devazepide; Donetidine; Etintidine Hydrochloride ; Famotidine; Fenmetozole Hydrochloride ; Flumazenil; Icatibant Acetate; Icotidine; Isradipine; Metiamide; Nadide; Nalmefene; Nalmexone Hydrochloride ; Naloxone Hydrochloride; Naltrexone; Nilvadipine;

Oxilorphan; Oxmetidine Hydrochloride ; Oxmetidine Mesylate ; Quadazocine Mesylate; Ranitidine; Ranitidine Bismuth Citrate ; Ranitidine Hydrochloride ; Sufotidine; Teludipine Hydrochloride; Tiapamil Hydrochloride; Tiotidine; Vapiprost Hydrochloride; Zaltidine Hydrochloride.

Anterior pituitary activator: Epimestrol.

Anterior pituitary suppressant: Danazol.

Anthelmintic: Albendazole; Anthelmycin; Bromoxanide; Bunamidine Hydrochloride; Butonate; Cambendazole; Carbantel Lauryl Sulfate; Clioxanide; Closantel; Cyclobendazole; Dichlorvos; Diethylcarbamazine Citrate; Dribendazole; Dymanthine Hydrochloride; Etibendazole; Fenbendazole; Furodazole; Hexylresorcinol; Mebendazole; Morantel Tartrate; Niclosamide; Nitramisole Hydrochloride; Nitrodan; Oxantel Pamoate; Oxfendazole; Oxibendazole; Parbendazole; Piperamide Maleate; Piperazine; Piperazine Citrate; Piperazine Edetate Calcium; Proclonol; Pyrantel Pamoate; Pyrantel Tartrate; Pyrvinium Pamoate; Rafoxanide; Stilbazium Iodide; Tetramisole Hydrochloride; Thiabendazole; Ticarbodine; Tioxidazole; Triclofenol Piperazine; Vincofos; Zilantel.

Anti-acne: Adapalene; Erythromycin Salnacedin; Inocoterone Acetate.

Anti-adrenergic: Acebutolol; Alprenolol Hydrochloride; Atenolol; Bretylium Tosylate; Bunolol Hydrochloride; Carteolol Hydrochloride; Celiprolol Hydrochloride; Cetamolol Hydrochloride; Cicloprolol Hydrochloride; Dexpropranolol Hydrochloride; Diacetolol Hydrochloride; Dihydroergotamine Mesylate; Dilevalol Hydrochloride; Esmolol Hydrochloride; Exaprolol Hydrochloride; Fenspiride Hydrochloride; Flestolol Sulfate; Labetalol Hydrochloride ; Levobetaxolol Hydrochloride; Levobunolol Hydrochloride; Metalol Hydrochloride; Metoprolol; Metoprolol Tartrate; Nadolol; Pamatolol Sulfate; Penbutolol Sulfate; Phentolamine Mesylate; Practolol; Propranolol Hydrochloride; Proroxan Hydrochloride; Solypertine Tartrate; Sotalol Hydrochloride; Timolol; Timolol Maleate; Tiprenolol Hydrochloride; Tolamolol; Zolertine Hydrochloride.

Anti-allergic: Amlexanox; Astemizole; Azclastine Hydrochloride; Eclazolast ; Minocromil ; Nedocromil ; Nedocromil Calcium ; Nedocromil Sodium ; Nivimedone Sodium; Pemirolast

Potassium ; Pentigetide; Pirquinozol; Poisonoak Extract; Probicromil Calcium; Proxicromil; Repirinast ; Tetrazolast Meglumine; Thiazinamium Chloride; Tiacrilast; Tiacrilast Sodium; Tiprinast Meglumine; Tixanox.

Anti-amebic : Berythromycin ; Bialamicol Hydrochloride; Chloroquine; Chloroquine Hydrochloride; Chloroquine Phosphate ; Clamoxyquin Hydrochloride; Clioquinol ; Emetine Hydrochloride; Iodoquinol; Paromomycin Sulfate; Quinfamide; Symetine Hydrochloride; Teclozan; Tetracycline ; Tetracycline Hydrochloride.

Anti-androgen: Benorterone; Cioteronel; Cyproterone Acetate; Delmadinone Acetate ; Oxendolone; Topterone; Zanoterone.

Anti-anemic: Epoetin Alfa; Epoetin Beta ; Ferrous Sulfate, Dried; Leucovorin Calcium.

Anti-anginal: Amlodipine Besylate; Amlodipine Maleate; Betaxolol Hydrochloride ; Bevantolol Hydrochloride ; Butoprozine Hydrochloride; Carvedilol ; Cinepazet Maleate; Metoprolol Succinate ; Molsidomine ; Monatepil Maleate; Primidolol ; Ranolazine Hydrochloride; Tosifen; Verapamil Hydrochloride.

Anti-anxiety agent: Adatanserin Hydrochloride; Alpidem; Binospirone Mesylate; Bretazenil; Glemanserin; Ipsapirone Hydrochloride; Mirisetron Maleate; Ocinaplon; Ondansetron Hydrochloride ; Panadiplon; Pancopride ; Pazinaclone; Serazapine Hydrochloride; Tandospirone Citrate; Zalospirone Hydrochloride.

Anti-arthritic: Lodelaben .

Anti-asthmatic: Ablukast; Ablukast Sodium; Azelastine Hydrochloride ; Bunaprolast; Cinalukast; Cromitrile Sodium; Cromolyn Sodium; Enofelast; Isamoxole; Ketotifen Fumarate; Levcromakalim; Lodoxamide Ethyl ; Lodoxamide Tromethamine; Montelukast Sodium; Ontazolast; Oxarbazole; Oxatomide; Piriprost; Piriprost Potassium; Pirolate; Pobilukast Edamine; Quazolast ; Repirinast ; Ritolukast; Sulukast; Tetrazolast Meglumine ; Tiaramide Hydrochloride; Tibenclast Sodium ; Tomelukast; Tranilast; Verlukast; Verofylline ; Zarirlukast.

Anti-atherosclerotic: Mifobate; Timefurone.

Antibacterial: Acedapsone ; Acetosulfone Sodium; Alamecin; Alexidine; Amdinocillin; Amdinocillin Pivoxil; Amicycline; Amifloxacin; Amifloxacin Mesylate; Amikacin; Amikacin Sulfate; Aminosalicylic acid; Aminosalicylate sodium; Amoxicillin; Amphomycin; Ampicillin; Ampicillin Sodium; Apalcillin Sodium; Apramycin; Aspartoein; Astromicin Sulfate; Avilamycin; Avoparcin; Azithromycin; Azlocillin; Azlocillin Sodium; Bacampicillin Hydrochloride; Bacitracin; Bacitraein Methylene Disalicylate; Baeitraein Zinc; Bambermyeins; Benzoylpas Calcium; Berythromyein ; Betamiein Sulfate; Biapenem; Biniramycin; Biphenamine Hydroehloride ; Bispyrithione Magsulfex ; Butikaein; Butirosin Sulfate; Capreomycin Sulfate; Carbadox; Carbenieillin Disodium; Carbenicillin Indanyl Sodium; Carbenicillin Phenyl Sodium; Carbenicillin Potassium; Carumonam Sodium; Cefaclor; Cefadroxil; Cefamandole; Cefamandole Nafate; Cefamandole Sodium; Cefaparole; Cefatrizine; Cefazaflur Sodium; Cefazolin; Cefazolin Sodium; Cefbuperazone; Cefdinir; Cefepime; Cefepime Hydroehloride; Cefetecol; Cefixime; Cefmenoxime Hydrochloride; Cefmetazole; Cefmetazole Sodium; Cefonicid Monosodium; Cefonicid Sodium; Cefoperazone Sodium; Ceforanide; Cefotaxime Sodium; Cefotetan; Cefotetan Disodium; Cefotiam Hydrochloride; Cefoxitin; Cefoxitin Sodium; Cefpimizole; Cefpimizole Sodium; Cefpiramide; Cefpiramide Sodium; Cefpirome Sulfate; Cefpodoxime Proxetil; Cefprozil; Cefroxadine; Cefsulodin Sodium; Ceftazidime; Ceftibuten; Ceftizoxime Sodium; Ceftriaxone Sodium; Cefuroxime; Cefuroxime Axetil; Cefuroxime Pivoxetil; Cefuroxime Sodium; Cephacetrile Sodium; Cephalexin; Cephalexin Hydrochloride; Cephaloglycin; Cephaloridine; Cephalothin Sodium; Cephapirin Sodium; Cephradine; Cetocycline Hydrochloride; Cetophenicol; Chloramphenicol; Chloramphenicol Palmitate; Chloramphenicol Pantothenate Complex ; Chloramphenicol Sodium Succinate; Chlorhexidine Phosphanilate; Chloroxylenol; Chlortetraeycline Bisulfate ; Chlortetraeycline Hydrochloride ; Cinoxacin; Ciprofloxacin; Ciprofloxacin Hydrochloride; Cirolemycin ; Clarithromyein; Clinafloxaein Hydrochloride; Clindamycin; Clindamycin Hydrochloride; Clindamycin Palmitate Hydrochloride; Clindamycin Phosphate; Clofazimine ; Cloxacillin Benzathine; Cloxacillin Sodium; Cloxyquin; Colistimethate Sodium; Colistin Sulfate; Coumermycin; Coumermycin Sodium; Cyclacillin; Cycloserine; Dalfopristin; Dapsone ; Daptomycin; Demeclocycline; Demeclocycline Hydrochloride; Demecycline; Denofungin ; Diaveridine; Dicloxacillin; Dicloxacillin Sodium; Dihydrostreptomycin Sulfate; Dipyrithione; Dirithromyein; Doxycycline; Doxycycline Calcium ; Doxycycline Fosfatex; Doxycycline Hyclate;

Droxacin Sodium; Enoxacin; Epicillin; Epitetracycline Hydrochloride; Erythromycin; Erythromycin Acistrate; Erythromycin Estolate; Erythromycin Ethylsuccinate; Erythromycin Gluceptate; Erythromycin Lactobionate; Erythromycin Propionate; Erythromycin Stearate; Ethambutol Hydrochloride; Ethionamide; Fleroxacin; Floxacillin; Fludalanine; Flumequine; Fosfomycin; Fosfomycin Tromethamine; Fumoxicillin; Furazolium Chloride; Furazolium Tartrate; Fusidate Sodium; Fusidic Acid; Gentamicin Sulfate; Gloximonam; Gramicidin; Haloprogin; Hetacillin; Hetacillin Potassium; Hexedine; Ibafloxacin; Imipenem; Isoconazole; Isepamicin; Isoniazid; Josamycin; Kanamycin Sulfate; Kitasamycin; Levofuraltadone; Levopropylcillin Potassium; Lexithromycin; Lincomycin; Lincomycin Hydrochloride; Lomefloxacin; Lomefloxacin Hydrochloride; Lomefloxacin Mesylate; Loracarbef; Mafenide; Meclocycline; Meclocycline Sulfosalicylate; Megalomicin Potassium Phosphate; Mequidox; Meropenem; Methacycline; Methacycline Hydrochloride; Methenamine; Methenamine Hippurate; Methenamine Mandelate; Methicillin Sodium; Metioprim; Metronidazole Hydrochloride; Metronidazole Phosphate; Mezlocillin; Mezlocillin Sodium; Minocycline; Minocycline Hydrochloride; Mirincamycin Hydrochloride ; Monensin ; Monensin Sodium ; Nafcillin Sodium; Nalidixate Sodium; Nalidixic Acid; Natamycin; Nebramycin; Neomycin Palmitate; Neomycin Sulfate; Neomycin Undecylenate ; Netilmicin Sulfate; Neutramycin; Nifuradene; Nifuraldezone; Nifuratel ; Nifuratrone; Nifurdazil; Nifurimide; Nifurpirinol; Nifurquinazol; Nifurthiazole; Nitrocycline; Nitrofurantoin; Nitromide; Norfloxacin; Novobiocin Sodium; Ofloxacin; Ormetoprim; Oxacillin Sodium; Oximonam; Oximonam Sodium; Oxolinic Acid; Oxytetracycline; Oxytetracycline Calcium; Oxytetracycline Hydrochloride; Paldimycin; Parachlorophenol; Paulomycin; Pefloxacin; Pefloxacin Mesylate; Penamecillin; Penicillin G Benzathine; Penicillin G Potassium; Penicillin G Procaine; Penicillin G Sodium; Penicillin V; Penicillin V Benzathine; Penicillin V Hydrabamine; Penicillin V Potassium; Pentizidone Sodium; Phenyl Aminosalicylate; Piperacillin Sodium; Pirbenicillin Sodium; Piridicillin Sodium; Pirlimycin Hydrochloride; Pivampicillin Hydrochloride; Pivampicillin Pamoate; Pivampicillin Probenate; Polymyxin B Sulfate; Porfiromycin ; Propikacin; Pyrazinamide; Pyrithione Zinc; Quindecamine Acetate; Quinupristin; Racephenicol; Ramoplanin; Ranimycin; Relomycin; Repromicin; Rifabutin; Rifametane; Rifamexil; Rifamide; Rifampin; Rifapentine; Rifaximin; Rolitetracycline; Rolitetracycline Nitrate; Rosaramicin; Rosaramicin Butyrate; Rosaramicin Propionate; Rosaramicin Sodium Phosphate; Rosaramicin Stearate; Rosoxacin; Roxarsone; Roxithromycin; Sancycline; Sanfetrinem Sodium; Sarmoxicillin; Sarpicillin; Scopafungin ; Sisomicin; Sisomicin Sulfate; Sparfloxacin; Spectinomycin Hydrochloride; Spiramycin; Stallimycin

Hydrochloride; Steffimycin; Streptomycin Sulfate; Streptonicozid; Sulfabenz ; Sulfabenzamide; Sulfacetamide; Sulfacetamide Sodium; Sulfacytine; Sulfadiazine; Sulfadiazine Sodium; Sulfadoxine; Sulfalene; Sulfamerazine; Sulfameter; Sulfamethazine; Sulfamethizole; Sulfamethoxazole; Sulfamonomethoxine; Sulfamoxole; Sulfanilate Zinc; Sulfanitran ; Sulfasalazine; Sulfasomizole; Sulfathiazole; Sulfazamet; Sulfisoxazole; Sulfisoxazole Acetyl; Sulfisoxazole Diolamine; Sulfomyxin; Sulopenem; Sultamicillin; Suncillin Sodium; Talampicillin Hydrochloride; Teicoplanin; Temafloxacin Hydrochloride; Temocillin; Tetracycline; Tetracycline Hydrochloride ; Tetracycline Phosphate Complex; Tetroxoprim; Thiamphenicol; Thiphencillin Potassium; Ticarcillin Cresyl Sodium; Ticarcillin Disodium; Ticarcillin Monosodium; Ticlatone; Tiodonium Chloride; Tobramycin; Tobramycin Sulfate; Tosufloxacin; Trimethoprim; Trimethoprim Sulfate; Trisulfapyrimidines; Troleandomycin; Trospectomycin Sulfate; Tyrothricin; Vancomycin; Vancomycin Hydrochloride; Virginiamycin; Zorbamycin.

Anticholelithic: Monoctanoin.

Anticholelithogenic: Chenodiol; Ursodiol.

Anticholinergic: Alverine Citrate; Anisotropine Methylbromide; Atropine; Atropine Oxide Hydrochloride; Atropine Sulfate; Belladonna; Benapryzine Hydrochloride; Benzetimide Hydrochloride; Benzilonium Bromide; Biperiden ; Biperiden Hydrochloride; Biperiden Lactate ; Clidinium Bromide; Cyclopentolate Hydrochloride; Dexetimide; Dicyclomine Hydrochloride; Dihexyverine Hydrochloride; Domazoline Fumarate; Elantrine; Elucaine; Ethybenztropine; Eucatropine Hydrochloride; Glycopyrrolate; Heteronium Bromide; Homatropine Hydrobromide; Homatropine Methylbromide; Hyoscyamine; Hyoscyamine Hydrobromide; Hyoscyamine Sulfate; Isopropamide Iodide; Mepenzolate Bromide; Methylatropine Nitrate; Metoquizine; Oxybutynin Chloride; Parapenzolate Bromide; Pentapiperium Methylsulfate; Phencarbamide; Poldine Methylsulfate; Proglumide; Propanthelinc Bromide; Propenzolate Hydrochloride; Scopolamine Hydrobromide; Tematropium Methylsulfate; Tiquinamide Hydrochloride; Tofenacin Hydrochloride; Toquizine; Triampyzine Sulfate; Trihexyphenidyl Hydrochloride; Tropicamide.

Anticoagulant: Ancrod; Anticoagulant Citrate Dextrose Solution ; Anticoagulant Citrate Phosphate Dextrose Adenine Solution; Anticoagulant Citrate Phosphate Dextrose Solution; Anticoagulant

Heparin Solution; Anticoagulant Sodium Citrate Solution; Ardeparin Sodium; Bivalirudin ; Bromindione; Dalteparin Sodium ; Desirudin; Dicumarol; Heparin Calcium; Heparin Sodium; Lyapolate Sodium; Nafamostat Mesylate ; Phenprocoumon; Tinzaparin Sodium ; Warfarin Sodium.

Anticoccidal: Maduramicin.

Anticonvulsant: Albutoin; Ameltolide; Atolide; Buramate; Carbamazepine ; Cinromide; Citenamide; Clonazepam; Cyheptamide; Dezinamide; Dimethadione; Divalprocx Sodium; Eterobarb; Ethosuximide; Ethotoin; Flurazepam Hydrochloride ; Fluzinamide; Fosphenytoin Sodium; Gabapentin; Ilepcimide; Lamotrigine; Magnesium Sulfate ; Mephenytoin; Mephobarbital ; Methetoin; Methsuximide; Milacemide Hydrochloride ; Nabazenil; Nafimidone Hydrochloride; Nitrazepam ; Phenacemide; Phenobarbital ; Phenobarbital Sodium ; Phensuximide; Phenytoin; Phenytoin Sodium; Primidone; Progabide; Ralitoline; Remacemide Hydrochloride; Ropizine; Sabeluzole ; Stiripentol; Sulthiame; Thiopental Sodium ; Tiletamine Hydrochloride ; Topiramate; Trimethadione; Valproate Sodium; Valproic Acid; Vigabatrin; Zoniclezole Hydrochloride; Zonisamide.

Antidepressant: Adatanserin Hydrochloride; Adinazolam ; Adinazolam Mesylate; Alaproclate; Aletamine Hydrochloride; Amedalin Hydrochloride; Amitriptyline Hydrochloride; Amoxapine; Aptazapine Maleate; Azaloxan Fumarate; Azepindole; Azipramine Hydrochloride; Bipenamol Hydrochloride; Bupropion Hydrochloride; Butacetin; Butriptyline Hydrochloride; Caroxazone; Cartazolate; Ciclazindol; Cidoxepin Hydrochloride; Cilobamine Mesylate; Clodazon Hydrochloride; Clomipramine Hydrochloride; Cotinine Fumarate; Cyclindole; Cypenamine Hydrochloride; Cyprolidol Hydrochloride; Cyproximide ; Daledalin Tosylate; Dapoxetine Hydrochloride; Dazadrol Maleate; Dazepinil Hydrochloride; Desipramine Hydrochloride; Dexamisole; Deximafen; Dibenzepin Hydrochloride; Dioxadrol Hydrochloride; Dothiepin Hydrochloride; Doxepin Hydrochloride; Duloxetine Hydrochloride; Eclanamine Maleate; Encyprate; Etoperidone Hydrochloride; Fantridone Hydrochloride; Fenmetozole Hydrochloride ; Fenmetramide; Fezolamine Fumarate; Fluotracen Hydrochloride ; Fluoxetine; Fluoxetine Hydrochloride; Fluparoxan Hydrochloride; Gamfexine; Guanoxyfen Sulfate ; Imafen Hydrochloride; Imiloxan Hydrochloride; Imipramine Hydrochloride; Indeloxazine Hydrochloride; Intriptyline Hydrochloride; Iprindole; Isocarboxazid; Ketipramine Fumarate; Lofepramine Hydrochloride; Lortalamine; Maprotiline;

Maprotiline Hydrochloride; Melitracen Hydrochloride; Milacemide Hydrochloride; Minaprine Hydrochloride; Mirtazapine; Moclobemide; Modaline Sulfate; Napactadine Hydrochloride; Napamezole Hydrochloride; Nefazodone Hydrochloride; Nisoxetine; Nitrafudam Hydrochloride; Nomifensine Maleate; Nortriptyline Hydrochloride; Octriptyline Phosphate; Opipramol Hydrochloride; Oxaprotiline Hydrochloride; Oxypertine; Paroxetine; Phenelzine Sulfate; Pirandamine Hydrochloride; Pizotyline ; Pridefine Hydrochloride; Prolintane Hydrochloride; Protriptyline Hydrochloride; Quipazine Maleate ; Rolicyprine; Seproxetine Hydrochloride; Sertraline Hydrochloride; Sibutramine Hydrochloride ; Sulpiride; Suritozole; Tametraline Hydrochloride; Tampramine Fumarate; Tandamine Hydrochloride; Thiazesim Hydrochloride; Thozalinone; Tomoxetine Hydrochloride; Trazodone Hydrochloride; Trebenzomine Hydrochloride; Trimipramine; Trimipramine Maleate; Venlafaxine Hydrochloride; Viloxazine Hydrochloride; Zimeldine Hydrochloride; Zometapine.

Antidiabetic: Acetohexamide; Buformin; Butoxamine Hydrochloride ; Camiglibose; Chlorpropamide; Ciglitazone; Englitazone Sodium; Etoformin Hydrochloride; Gliamilide; Glibornuride; Glicetanile Sodium; Gliflumide; Glipizide; Glucagon; Glyburide; Glyhexamide; Glymidine Sodium; Glyoctamide; Glyparamide; Insulin; Insulin, Dalanated; Insulin Human; Insulin Human, Isophane; Insulin Human Zinc; Insulin Human Zinc, Extended; Insulin, Isophane; Insulin Lispro; Insulin, Neutral; Insulin Zinc; Insulin Zinc, Extended; Insulin Zinc, Prompt; Linogliride; Linogliride Fumarate; Metformin; Methyl Palmoxirate; Palmoxirate Sodium; Pioglitazone Hydrochloride; Pirogliride Tartrate; Proinsulin Human; Seglitide Acetate; Tolazamide; Tolbutamide; Tolpyrramide; Troglitazone; Zopolrestat.

Antidiarrheal: Rolgamidine, Diphenoxylate hydrochloride (Lomotil), Metronidazole (Flagyl), Methylprednisolone (Medrol), Sulfasalazine (Azulfidine).

Antidiuretic: Argipressin Tannate; Desmopressin Acetate; Lypressin .

Antidote: Dimercaprol; Edrophonium Chloride; Fomepizole; Leucovorin Calcium ; Levoleucovorin Calcium; Methylene Blue ; Protamine Sulfate.

Antidyskinetic: Selegiline Hydrochloride .

Anti-emetic: Alosetron Hydrochloride; Batanopride Hydrochloride; Bemesetron; Benzquinamide; Chlorpromazine ; Chlorpromazine Hydrochloride ; Clebopride; Cyclizine Hydrochloride; Dimenhydrinate; Diphenidol; Diphenidol Hydrochloride; Diphenidol Pamoate; Dolasetron Mesylate ; Domperidone; Dronabinol; Fludorex; Flumeridone; Galdansetron Hydrochloride; Granisetron; Granisetron Hydrochloride; Lurosetron Mesylate; Meclizine Hydrochloride; Metoclopramide Hydrochloride; Metopimazine; Ondansetron Hydrochloride ; Pancopride; Prochlorperazine; Prochlorperazine Edisylate; Prochlorperazine Maleate ; Promethazine Hydrochloride ; Thiethylperazine; Thiethylperazine Malate; Thiethylperazine Maleate; Trimethobenzamide Hydrochloride; Zacopride Hydrochloride.

Anti-epileptic: Felbamate; Loreclezole; Tolgabide, lamotrigine.

Anti-estrogen: Clomctherone; Delmadinone Acetate ; Nafoxidine Hydrochloride; Nitromifene Citrate; Raloxifene Hydrochloride; Tamoxifen Citrate; Toremifene Citrate ; Trioxifene Mesylate.

Antifibrinolytic: Nafamostat Mesylate .

Antifungal: Acrisorcin; Ambruticin; Amphotericin B; Azaconazole; Azaserine; Basifungin; Bifonazole; Biphenamine Hydrochloride ; Bispyrithione Magsulfex ; Butoconazole Nitrate; Calcium Undecylenate; Candicidin; Carbol-Fuchsin; Chlordantoin; Ciclopirox; Ciclopirox Olamine; Cilofungin; Cisconazole; Clotrimazole; Cuprimyxin; Denofungin ; Dipyrithione; Doconazole; Econazole; Econazole Nitrate; Enilconazole; Ethonam Nitrate; Fenticonazole Nitrate; Filipin; Fluconazole; Flucytosine; Fungimycin; Griseofulvin; Hamycin; Isoconazole ; Itraconazole; Kalafungin; Ketoconazole; Lomofungin; Lydimycin; Mepartricin ; Miconazole; Miconazole Nitrate; Monensin ; Monensin Sodium ; Naftifine Hydrochloride; Neomycin Undecylenate ; Nifuratel ; Nifurmerone; Nitralamine Hydrochloride; Nystatin; Octanoic Acid; Orconazole Nitrate; Oxiconazole Nitrate; Oxifungin Hydrochloride; Parconazole Hydrochloride; Partricin ; Potassium Iodide ; Proclonol ; Pyrithione Zinc ; Pyrrolnitrin; Rutamycin; Sanguinarium Chloride ; Saperconazole; Scopafungin ; Selenium Sulfide ; Sinefungin; Sulconazole Nitrate; Terbinafine; Terconazole; Thiram; Ticlatone ; Tioconazole; Tolciclate; Tolindate; Tolnaftate; Triacetin; Triafungin; Undecylenic Acid; Viridofulvin; Zinc Undecylenate; Zinoconazole Hydrochloride.

Antiglaucoma agent : Alprenoxime Hydrochloride ; Colforsin; Dapiprazole Hydrochloride ; Dipivefrin Hydrochloride ; Naboctate Hydrochloride ; Pilocarpine; Pirnabine.

Antihemophilic: Antihemophilic Factor.

Antihemorrhagic: Poliglusam.

Antihemorrheologic:Phentoxifylline

Antihistaminic: Acrivastine; Antazoline Phosphate; Astemizole ; Azatadine Maleate; Barmastine; Bromodiphenhydramine Hydrochloride; Brompheniramine Maleate; Carbinoxamine Maleate; Cetirizine Hydrochloride; Chlorpheniramine Maleate; Chlorpheniramine Polistirex; Cinnarizine; Clemastine; Clemastine Fumarate; Closiramine Acceturate; Cycliramine Maleate; Cyclizine; Cyproheptadine Hydrochloride ; Dexbrompheniramine Maleate; Dexchlorpheniramine Maleate; Dimethindene Maleate; Diphenhydramine Citrate; Diphenhydramine Hydrochloride; Dorastine Hydrochloride; Doxylamine Succinate; Ebastine; Levocabastine Hydrochloride; Loratadine; Mianserin Hydrochloride ; Noberastine; Orphenadrine Citrate ; Pyrabrom; Pyrilamine Maleate; Pyroxamine Maleate; Rocastine Hydrochloride; Rotoxamine; Tazifylline Hydrochloride; Temelastine; Terfenadine; Tripclennamine Citrate; Tripelennamine Hydrochloride; Triprolidine Hydrochloride; Zolamine Hydrochloride .

Antihyperlipidemic: Cholestyramine Resin ; Clofibrate; Colestipol Hydrochloride; Crilvastatin; Dalvastatin; Dextrothyroxine Sodium; Fluvastatin Sodium ; Gemfibrozil; Lecimibide; Lovastatin ; Niacin ; Pravastatin Sodium; Probucol; Simvastatin; Tiqueside; Xenbucin.

Antihyperlipoproteinemic: Acifran; Beloxamide; Bezafibrate; Boxidine; Butoxamine Hydrochloride; Cetaben Sodium; Ciprofibrate; Gemcadiol; Halofenate ; Lifibrate; Meglutol; Nafenopin; Pimetine Hydrochloride; Theofibrate; Tibric Acid; Treloxinate.

Antihypertensive: Alfuzosin Hydrochloride; Alipamide ; Althiazide; Amiquinsin Hydrochloride; Amlodipine Besylate ; Amlodipine Maleate ; Anaritide Acetate ; Atiprosin Maleate; Belfosdil; Bemitradine; Bendacalol Mesylate; Bendroflumethiazide ; Benzthiazide ; Betaxolol Hydrochloride

; Bethanidine Sulfate; Bevantolol Hydrochloride ; Bielodil Hydrochloride; Bisoprolol Fumarate; Bucindolol Hydrochloride; Bupicomide; Buthiazide: Candoxatril; Candoxatrilat; Captopril ; Carvedilol ; Ceronapril; Chlorothiazide Sodium ; Cicletanine; Cilazapril; Clonidine; Clonidine Hydrochloride; Clopamide ; Cyclopenthiazide; Cyclothiazide ; Darodipine ; Debrisoquin Sulfate; Delapril Hydrochloride; Diapamide ; Diazoxide; Dilevalol Hydrochloride ; Diltiazem Hydrochloride; Diltiazem Malate; Ditekiren; Doxazosin Mesylate; Ecadotril; Enalapril Maleate; Enalaprilat; Enalkiren; Endralazine Mesylate; Epithiazide ; Eprosartan; Eprosartan Mesylate; Fenoldopam Mesylate ; Flavodilol Maleate; Flordipine; Flosequinan; Fosinopril Sodium ; Fosinoprilat; Guanabenz; Guanabenz Acetate; Guanacline Sulfate; Guanadrel Sulfate; Guancydine; Guanethidine Monosulfate; Guanethidine Sulfate; Guanfacine Hydrochloride; Guanisoquin Sulfate; Guanoclor Sulfate; Guanoctine Hydrochloride; Guanoxabenz; Guanoxan Sulfate; Guanoxyfen Sulfate ; Hydralazine Hydrochloride; Hydralazine Polistirex; Hydroflumethiazide ; Indacrinone ; Indapamide ; Indolapril Hydrochloride; Indoramin; Indoramin Hydrochloride; Indorenate Hydrochloride; Lacidipine; Leniquinsin; Levcromakalim ; Lisinopril; Lofexidine Hydrochloride; Losartan Potassium; Losulazine Hydrochloride; Mebutamate; Mecamylamine Hydrochloride; Medroxalol; Medroxalol Hydrochloride; Methalthiazide ; Methyclothiazide ; Methyldopa; Methyldopate Hydrochloride; Metipranolol; Metolazone ; Metoprolol Fumarate; Metoprolol Succinate ; Metyrosine; Minoxidil; Monatepil Maleate ; Muzolimine ; Nebivolol; Nifidipine; Nitrendipine; Ofornine; Pargyline Hydrochloride; Pazoxide; Pelanserin Hydrochloride ; Perindopril Erbumine; Phenoxybenzamine Hydrochloride; Pinacidil; Pivopril; Polythiazide ; Prazosin Hydrochloride; Primidolol ; Prizidilol Hydrochloride; Quinapril Hydrochloride ; Quinaprilat ; Quinazosin Hydrochloride; Quinelorane Hydrochloride ; Quinpirole Hydrochloride; Quinuclium Bromide; Ramipril ; Rauwolfia Serpentina; Reserpine; Saprisartan Potassium; Saralasin Acetate; Sodium Nitroprusside; Sulfinalol Hydrochloride; Tasosartan; Teludipine Hydrochloride ; Temocapril Hydrochloride; Terazosin Hydrochloride; Terlakiren; Tiamenidine; Tiamenidine Hydrochloride; Tierynafen ; Tinabinol; Tiodazosin; Tipentosin Hydrochloride; Trichlormethiazide ; Trimazosin Hydrochloride; Trimethaphan Camsylate; Trimoxamine Hydrochloride; Tripamide; Xipamide ; Zankiren Hydrochloride; Zofenoprilat Arginine.

Antihypotensive: Ciclafrine Hydrochloride; Midodrine Hydrochloride.

Anti-infective: Difloxacin Hydrochloride ; Lauryl Isoquinolinium Bromide; Moxalactam Disodium; Ornidazole; Pentisomicin; Sarafloxacin Hydrochloride; Protease inhibitors of HIV and other retroviruses; Integrase Inhibitors of HIV and other retroviruses; Cefaclor (Ceclor); Acyclovir (Zovirax); Norfloxacin (Noroxin); Cefoxitin (Mefoxin); Cefuroxime axetil (Ceftin); Ciprofloxacin (Cipro).

Anti-infective, topical: Alcohol; Aminacrine Hydrochloride; Benzethonium Chloride : Bithionolate Sodium; Bromchlorenone; Carbamide Peroxide; Cetalkonium Chloride; Cetylpyridinium Chloride : Chlorhexidine Hydrochloride; Clioquinol ; Domiphen Bromide; Fenticlor; Fludazonium Chloride; Fuchsin, Basic; Furazolidone ; Gentian Violet; Halquinols; Hexachlorophene : Hydrogen Peroxide; Ichthammol; Imidecyl Iodine; Iodine; Isopropyl Alcohol ; Mafenide Acetate; Meralein Sodium; Mercufenol Chloride; Mercury, Ammoniated; Methylbenzethonium Chloride; Nitrofurazone; Nitromersol; Octenidine Hydrochloride; Oxychlorosene; Oxychlorosene Sodium; Parachlorophenol, Camphorated; Potassium Permanganate; Povidone-Iodine; Sepazonium Chloride; Silver Nitrate; Sulfadiazine, Silver; Symclosene; Thimerfonate Sodium; Thimerosal : Troclosene Potassium.

Anti-inflammatory: Alclofenac; Alclometasone Dipropionate; Algestone Acetonide; Alpha Amylase; Amcinafal; Amcinafide; Amfenac Sodium; Amiprilose Hydrochloride; Anakinra; Anirolac ; Anitrazafen; Apazone; Balsalazide Disodium; Bendazac; Benoxaprofen ; Benzydamine Hydrochloride; Bromelains; Broperamole; Budesonide; Carprofen; Ciclopropfen; Cintazone; Cliprofen; Clobetasol Propionate; Clobetasone Butyrate; Clopirac; Cloticasone Propionate; Cormethasone Acetate; Cortodoxone; Deflazacort; Desonide; Desoximetasone; Dexamethasone Dipropionate; Diclofenac Potassium; Diclofenac Sodium; Diflorasone Diacetate; Diflumidone Sodium; Diflunisal ; Difluprednate; Diftalone; Dimethyl Sulfoxide; Drocinonide; Endrysone; Enlimomab ; Enolicam Sodium ; Epirizole ; Etodolac; Etofenamate ; Felbinac; Fenamole; Fenbufen; Fenclofenac; Fenclorac; Fendosal; Fenpipalone; Fentiazac; Flazalone; Fluazacort; Flufenamic Acid; Flumizole; Flunisolide Acetate; Flunixin ; Flunixin Meglumine ; Fluocortin Butyl; Fluorometholone Acetate; Fluquazone; Flurbiprofen ; Fluretofen; Fluticasone Propionate; Furaprofen; Furobufen; Halcinonide; Halobetasol Propionate; Halopredone Acetate; Ibufenac ; Ibuprofen; Ibuprofen Aluminum; Ibuprofen Piconol; Ilonidap; Indomethacin; Indomethacin Sodium; Indoprofen ; Indoxole ; Intrazole; Isoflupredone Acetate; Isoxepac; Isoxicam; Ketoprofen; Lofemizole Hydrochloride ; Lornoxicam ; Loteprednol Etabonate; Meclofenamate Sodium; Meclofenamic Acid;

Meclorisone Dibutyrate; Mefenamic Acid ; Mesalamine; Meseclazone; Methylprednisolone Suleptanate; Morniflumate; Nabumetone; Naproxen ; Naproxen Sodium ; Naproxol ; Nimazone; Olsalazine Sodium; Orgotein ; Orpanoxin; Oxaprozin; Oxyphenbutazone; Paranyline Hydrochloride; Pentosan Polysulfate Sodium; Phenbutazone Sodium Glycerate; Pirfenidone ; Piroxicam; Piroxicam Cinnamate; Piroxicam Olamine; Pirprofen; Prednazate; Prifelone; Prednisolone Sodium Phosphate; Prodolic Acid; Proquazone; Proxazole; Proxazole Citrate ; Rimexolone; Romazarit ; Salcolex ; Salnacedin; Salsalate ; Sanguinarium Chloride ; Seclazone ; Sermetacin; Sudoxicam; Sulindac; Suprofen; Talmetacin; Talniflumate ; Talosalate ; Tebufelone ; Tenidap; Tenidap Sodium; Tenoxicam; Tesicam; Tesimide; Tetrydamine ; Tiopinac ; Tixocortol Pivalate; Tolmetin; Tolmetin Sodium; Triclonide; Triflumidate; Zidometacin; Zomepirac Sodium .

Antikeratinizing agent: Doretinel; Linarotene; Pelretin.

Antimalarial : Acedapsone ; Amodiaquine Hydrochloride ; Amquinate; Arteflene; Chloroquine ; Chloroquine Hydrochloride ; Chloroquine Phosphate ; Cycloguanil Pamoate; Enpiroline Phosphate; Halofantrine Hydrochloride ; Hydroxychloroquine Sulfate ; Mefloquine Hydrochloride; Menoctone; Mirincamycin Hydrochloride ; Primaquine Phosphate; Pyrimethamine; Quinine Sulfate; Tebuquine.

Antimicrobial: Aztreonam; Chlorhexidine Gluconate; Imidurea; Lycetamine; Nibroxane; Pirazmonam Sodium; Propionic Acid ; Pyrithione Sodium; Sanguinarium Chloride ; Tigemonam Dicholine.

Antimigraine: Dolasetron Mesylate ; Naratriptan Hydrochloride; Sergolexole Maleate; Sumatriptan Succinate; Zatosetron Maleate.

Antimitotic: Podofilox.

Antimycotic: Amorolfine.

Antinauseant : Buclizine Hydrochloride ; Cyclizine Lactate; Naboctate Hydrochloride .

Antineoplastic: Acivicin; Aclarubicin; Acodazole Hydrochloride; Acronine; Adozelesin; Aldesleukin ; Altretamine; Ambomycin; Ametantrone Acetate; Aminoglutethimide ; Amsacrine; Anastrozole; Anthramycin; Asparaginase; Asperlin ; Azacitidine; Azetepa; Azotomycin; Batimastat; Benzodepa; Bicalutamide; Bisantrene Hydrochloride; Bisnafide Dimesylate; Bizelesin; Bleomycin Sulfate; Brequinar Sodium; Bropirimine ; Busulfan; Cactinomycin; Calusterone; Caracemide; Carbetimer; Carboplatin; Carmustine; Carubicin Hydrochloride; Carzelesin; Cedefingol; Chlorambucil; Cirolemycin ; Cisplatin; Cladribine; Crisnatol Mesylate; Cyclophosphamide ; Cytarabine ; Dacarbazine; Dactinomycin; Daunorubicin Hydrochloride; Decitabine; Dexormaplatin; Dezaguanine; Dezaguanine Mesylate; Diaziquone; Docetaxel; Doxorubicin; Doxorubicin Hydrochloride; Droloxifene; Droloxifene Citrate; Dromostanolone Propionate; Duazomycin; Edatrexate; Eflornithine Hydrochloride ; Elsamitrucin; Enloplatin; Enpromate; Epipropidine; Epirubicin Hydrochloride; Erbulozole; Esorubicin Hydrochloride; Estramustine; Estramustine Phosphate Sodium; Etanidazole; Ethiodized Oil I 131; Etoposide; Etoposide Phosphate; Etoprine; Fadrozole Hydrochloride; Fazarabine; Fenretinide; Floxuridine ; Fludarabine Phosphate; Fluorouracil; Flurocitabine; Fosquidone; Fostriecin Sodium; Gemcitabine; Gemcitabine Hydrochloride; Gold Au 198 ; Hydroxyurea; Idarubicin Hydrochloride; Ifosfamide; Ilmofosine; Isotretinoin; Interferon Alfa-2a ; Interferon Alfa-2b ; Interferon Alfa-n1; Interferon Alfa-n3; Interferon Beta- I a ; Interferon Gamma- I b; Iproplatin; Irinotecan Hydrochloride ; Lanreotide Acetate; Letrozole; Leuprolide Acetate ; Liarozole Hydrochloride; Lometrexol Sodium; Lomustine; Losoxantrone Hydrochloride; Masoprocol; Maytansine; Mechlorethamine Hydrochloride; Megestrol Acetate; Melengestrol Acetate; Melphalan; Menogaril; Mercaptopurine; Methotrexate; Methotrexate Sodium; Metoprine; Meturedepa; Mitindomide; Mitocarcin; Mitocromin; Mitogillin; Mitomalcin; Mitomycin; Mitosper; Mitotane; Mitoxantrone Hydrochloride; Mycophenolic Acid; Nocodazole; Nogalamycin; Ormaplatin; Oxisuran; Paclitaxel; Pegaspargase; Peliomycin; Pentamustine; Peplomycin Sulfate; Perfosfamide; Pipobroman; Piposulfan; Piroxantrone Hydrochloride; Plicamycin; Plomestane; Porfimer Sodium; Porfiromycin ; Prednimustine; Procarbazine Hydrochloride; Puromycin ; Puromycin Hydrochloride; Pyrazofurin; Riboprine; Rogletimide; Safingol ; Safingol Hydrochloride ; Semustine; Simtrazene; Sparfosate Sodium; Sparsomycin; Spirogermanium Hydrochloride; Spiromustine; Spiroplatin; Streptonigrin; Streptozocin; Strontium Chloride Sr 89; Sulofenur; Talisomycin; Taxane; Taxoid; Tecogalan Sodium; Tegafur; Teloxantrone Hydrochloride; Temoporfin; Teniposide; Teroxirone; Testolactone; Thiamiprine; Thioguanine; Thiotepa; Tiazofurin; Tirapazamine; Topotecan Hydrochloride; Toremifene Citrate; Trestolone

Acetate; Triciribine Phosphate; Trimetrexate; Trimetrexate Glucuronate; Triptorelin; Tubulozole Hydrochloride; Uracil Mustard; Uredepa; Vapreotide; Verteporfin; Vinblastine Sulfate; Vincristine Sulfate; Vindesine; Vindesine Sulfate; Vinepidine Sulfate; Vinglycinate Sulfate; Vinleurosine Sulfate; Vinorelbine Tartrate; Vinrosidine Sulfate; Vinzolidine Sulfate; Vorozole; Zeniplatin; Zinostatin; Zorubicin Hydrochloride.

Other anti-neoplastic compounds include: 20-epi-1,25 dihydroxyvitamin D3; 5-ethynyluracil; abiraterone; aclarubicin; acylfulvene; adecypenol; adozelesin; aldesleukin; ALL-TK antagonists; altretamine; ambamustine; amidox; amifostine; aminolevulinic acid; amrubicin; amsacrine; anagrelide; anastrozole; andrographolide; angiogenesis inhibitors; antagonist D; antagonist G; antarelix; anti-dorsalizing morphogenetic protein-1; antiandrogen, prostatic carcinoma; antiestrogen; antineoplaston; antisense oligonucleotides; aphidicolin glycinate; apoptosis gene modulators; apoptosis regulators; apurinic acid; ara-CDP-DL-PTBA; arginine deaminase; asulacrine; atamestane; atrimustine; axinastatin 1; axinastatin 2; axinastatin 3; azasetron; azatoxin; azatyrosine; baccatin III derivatives; balanol; batimastat; BCR/ABL antagonists; benzochlorins; benzoylstaurosporine; beta lactam derivatives; beta-alethine; betaclamycin B; betulinic acid; bFGF inhibitor; bicalutamide; bisantrene; bisaziridinylspermine; bisnafide; bistratene A; bizelesin; breflate; bropirimine; budotitane; buthionine sulfoximine; calcipotriol; calphostin C; camptothecin derivatives; canarypox IL-2; capecitabine; carboxamide-amino-triazole; carboxyamidotriazole; CaRest M3; CARN 700; cartilage derived inhibitor; carzelesin; casein kinase inhibitors (ICOS); castanospermine; cecropin B; cetrorelix; chlorins; chloroquinoxaline sulfonamide; cicaprost; cis-porphyrin; cladribine; clomifene analogues; clotrimazole; collismycin A; collismycin B; combretastatin A4; combretastatin analogue; conagenin; crambescidin 816; crisnatol; cryptophycin 8; cryptophycin A derivatives; curacin A; cyclopentanthraquinones; cycloplatam; cypemycin; cytarabine ocfosfate; cytolytic factor; cytostatin; dacliximab; decitabine; dehydrodidemnin B; deslorelin; dexifosfamide; dexrazoxane; dexverapamil; diaziquone; didemnin B; didox; diethylnorspermine; dihydro-5-azacytidine; dihydrotaxol, 9-; dioxamycin; diphenyl spiromustine; docosanol; dolasetron; doxifluridine; droloxifene; dronabinol; duocarmycin SA; ebselen; ecomustine; edelfosine; edrecolomab; eflornithine; elemene; emitefur; epirubicin; epristeride; estramustine analogue; estrogen agonists; estrogen antagonists; etanidazole; etoposide phosphate; exemestane; fadrozole; fazarabine; fenretinide; filgrastim; finasteride; flavopiridol; flezelastine; fluasterone; fludarabine; fluorodaunorunicin hydrochloride; forfenimex; formestane; fostriecin; fotemustine; gadolinium texaphyrin; gallium nitrate; galocitabine; ganirelix; gelatinase inhibitors; gemcitabine; glutathione

inhibitors; hepsulfam; heregulin; hexamethylene bisacetamide; hypericin; ibandronic acid; idarubicin; idoxifene; idramantone; ilmofosine; ilomastat; imidazoacridones; imiquimod; immunostimulant peptides; insulin-like growth factor-1 receptor inhibitor; interferon agonists; interferons; interleukins; iobenguane; iododoxorubicin; ipomeanol, 4-; irinotecan; iroplact; irsogladine; isobengazole; isohomohalicondrin B; itasetron; jasplakinolide; kahalalide F; lamellarin-N triacetate; lanreotide; leinamycin; lenograstim; lentinan sulfate; leptolstatin; letrozole; leukemia inhibiting factor; leukocyte alpha interferon; leuprolide + estrogen + progesterone; leuprorelin; levamisole; liarozole; linear polyamine analogue; lipophilic disaccharide peptide; lipophilic platinum compounds; lissoclinamide 7; lobaplatin; lombricine; lometrexol; lonidamine; losoxantrone; lovastatin; loxoribine; lurtotecan; lutetium texaphyrin; lysofylline; lytic peptides; maitansine; mannostatin A; marimastat; masoprocol; maspin; matrilysin inhibitors; matrix metalloproteinase inhibitors; menogaril; merbarone; meterelin; methioninase; metoclopramide; MIF inhibitor; mifepristone; miltefosine; mirimostim; mismatched double stranded RNA; mitoguazone; mitolactol; mitomycin analogues; mitonafide; mitotoxin fibroblast growth factor-saporin; mitoxantrone; mofarotene; molgramostim; monoclonal antibody, human chorionic gonadotrophin; monophosphoryl lipid A + myobacterium cell wall sk; mopidamol; multiple drug resistance gene inhibitor; multiple tumor suppressor 1-based therapy; mustard anticancer agent; mycaperoxide B; mycobacterial cell wall extract; myriaporone; N-acetyldinaline; N-substituted benzamides; nafarelin; nagrestip; naloxone + pentazocine; napavin; naphterpin; nartograstim; nedaplatin; nemorubicin; neridronic acid; neutral endopeptidase; nilutamide; nisamycin; nitric oxide modulators; nitroxide antioxidant; nitrullyn; O6-benzylguanine; octreotide; okicenone; oligonucleotides; onapristone; ondansetron; ondansetron; oracin; oral cytokine inducer; ormaplatin; osaterone; oxaliplatin; oxaunomycin; paclitaxel analogues; paclitaxel derivatives; palauamine; palmitoylrhizoxin; pamidronic acid; panaxytriol; panomifene; parabactin; pazelliptine; pegaspargase; peldesine; pentosan polysulfate sodium; pentostatin; pentrozole; perflubron; perfosfamide; perillyl alcohol; phenazinomycin; phenylacetate; phosphatase inhibitors; picibanil; pilocarpine hydrochloride; pirarubicin; piritrexim; placetin A; placetin B; plasminogen activator inhibitor; platinum complex; platinum compounds; platinum-triamine complex; porfimer sodium; porfiromycin; propyl bis-acridone; prostaglandin J2; proteasome inhibitors; protein A-based immune modulator; protein kinase C inhibitor; protein kinase C inhibitors, microalgal; protein tyrosine phosphatase inhibitors; purine nucleoside phosphorylase inhibitors; purpurins; pyrazoloacridine; pyridoxylated hemoglobin polyoxyethylene conjugate; raf antagonists; raltitrexed; ramosetron; ras farnesyl protein transferase

inhibitors; ras inhibitors; ras-GAP inhibitor; retelliptine demethylated; rhenium Re 186 etidronate; rhizoxin; ribozymes; RII retinamide; rogletimide; rohitukine; romurtide; roquinimex; rubiginone B1; ruboxyl; safingol; saintopin; SarCNU; sarcophytol A; sargramostim; Sdi 1 mimetics; semustine; senescence derived inhibitor 1; sense oligonucleotides; signal transduction inhibitors; signal transduction modulators; single chain antigen binding protein; sizofiran; sobuzoxane; sodium borocaptate; sodium phenylacetate; solverol; somatomedin binding protein; sonermin; sparfosic acid; spicamycin D; spiromustine; splenopentin; spongistatin 1; squalamine; stem cell inhibitor; stem-cell division inhibitors; stipiamide; stromelysin inhibitors; sulfinosine; superactive vasoactive intestinal peptide antagonist; suradista; suramin; swainsonine; synthetic glycosaminoglycans; tallimustine; tamoxifen methiodide; tauromustine; tazarotene; tecogalan sodium; tegafur; tellurapyrylium; telomerase inhibitors; temoporfin; temozolomide; teniposide; tetrachlorodecaoxide; tetrazomine; thaliblastine; thalidomide; thiocoraline; thrombopoietin; thrombopoietin mimetic; thymalfasin; thymopoietin receptor agonist; thymotrinan; thyroid stimulating hormone; tin ethyl etiopurpurin; tirapazamine; titanocene dichloride; topotecan; topsentin; toremifene; totipotent stem cell factor; translation inhibitors; tretinoin; triacetyluridine; triciribine; trimetrexate; triptorelin; tropisetron; turosteride; tyrosine kinase inhibitors; tyrphostins; UBC inhibitors; ubenimex; urogenital sinus-derived growth inhibitory factor; urokinase receptor antagonists; vapreotide; variolin B; vector system, erythrocyte gene therapy; velaresol; veramine; verdins; verteporfin; vinorelbine; vinxaltine; vitaxin; vorozole; zanoterone; zeniplatin; zilascorb; zinostatin stimalamer.

Anti-cancer Supplementary Potentiating Agents: Tricyclic anti-depressant drugs (e.g., imipramine, desipramine, amitryptyline, clomipramine, trimipramine, doxepin, nortriptyline, protriptyline, amoxapine and maprotiline); non-tricyclic anti-depressant drugs (e.g., sertraline, trazodone and citalopram); Ca^{++} antagonists (e.g., verapamil, nifedipine, nitrendipine and caroverine); Calmodulin inhibitors (e.g., prenylamine, trifluoroperazine and clomipramine); Amphotericin B; Triparanol analogues (e.g., tamoxifen); antiarrhythmic drugs (e.g., quinidine); antihypertensive drugs (e.g., reserpine); Thiol depleters (e.g., buthionine and sulfoximine) and Multiple Drug Resistance reducing agents such as Cremaphor EL. The compounds of the invention also can be administered with cytokines such as granulocyte colony stimulating factor.

Antineutropenic: Filgrastim; Lenograstim; Molgramostim; Regramostim; Sargramostim.

Antiobsessional agent: Fluvoxamine Maleate.

Antiparasitic: Abamectin; Clorsulon; Ivermectin.

Antiparkinsonian: Benztropine Mesylate; Biperiden; Biperiden Hydrochloride; Biperiden Lactate; Carbidopa-Levodopa; Carmantadine; Ciladopa Hydrochloride; Dopamantine; Ethopropazine Hydrochloride; Lazabemide; Levodopa; Lometraline Hydrochloride; Mofegiline Hydrochloride; Naxagolide Hydrochloride; Pareptide Sulfate; Procyclidine Hydrochloride; Quinelorane Hydrochloride; Ropinirole Hydrochloride; Selegiline Hydrochloride; Tolcapone; Trihexyphenidyl Hydrochloride.

Antiperistaltic: Difenoximide Hydrochloride; Difenoxin; Diphenoxylate Hydrochloride; Fluperamide; Lidamidine Hydrochloride; Loperamide Hydrochloride; Malethamer; Nufenoxole; Paregoric.

Antipneumocystic: Atovaquone.

Antiproliferative agent: Piritrexim Isethionate.

Antiprostatic hypertrophy: Sitogluside.

Antiprotozoal: Amodiaquine; Azanidazole; Bamnidazole; Carnidazole; Chlortetracycline Bisulfate ; Chlortetracycline Hydrochloride; Flubendazole; Flunidazole; Halofuginone Hydrobromide; Imidocarb Hydrochloride; Ipronidazole; Metronidazole; Misonidazole; Moxnidazole; Nitarsone; Partricin; Puromycin; Puromycin Hydrochloride; Ronidazole; Sulnidazole; Tinidazole.

Antipruritic: Cyproheptadine Hydrochloride ; Methdilazine; Methdilazine Hydrochloride; Trimeprazine Tartrate.

Antipsoriatic: Acitretin; Anthralin; Azaribine; Calcipotriene; Cycloheximide; Enazadrem Phosphate; Etretinate; Liarozole Fumarate; Lonapalene; Tepoxalin.

Antipsychotic: Acetophenazine Malcate; Alentemol Hydrobromide; Alpertine; Azaperone; Batelapine Maleate; Benperidol; Benzindopyrine Hydrochloride; Brofoxine; Bromperidol;

Bromperidol Decanoate; Butaclamol Hydrochloride; Butaperazine; Butaperazine Maleate; Carphenazine Maleate; Carvotroline Hydrochloride; Chlorpromazine; Chlorpromazine Hydrochloride; Chlorprothixene; Cinperene; Cintriamide; Clomacran Phosphate; Clopenthixol; Clopimozide; Clopipazan Mesylate; Cloroperone Hydrochloride; Clothiapine; Clothixamide Maleate; Clozapine; Cyclophenazine Hydrochloride; Droperidol; Etazolate Hydrochloride; Fenimide; Flucindole; Flumezapine; Fluphenazine Decanoate; Fluphenazine Enanthate; Fluphenazine Hydrochloride; Fluspiperone; Fluspirilene; Flutroline; Gevotroline Hydrochloride; Halopemide; Haloperidol; Haloperidol Decanoate; Iloperidone; Imidoline Hydrochloride; Lenperone; Mazapertine Succinate; Mesoridazine; Mesoridazine Besylate; Metiapine; Milenperone; Milipertine; Molindone Hydrochloride; Naranol Hydrochloride; Neflumozide Hydrochloride; Ocaperidone; Olanzapine; Oxiperomide; Penfluridol; Pentiapine Maleate; Perphenazine; Pimozide; Pinoxepin Hydrochloride; Pipamperone; Piperacetazine; Pipotiazine Palmitate; Piquindone Hydrochloride; Prochlorperazine Edisylate; Prochlorperazine Maleate; Promazine Hydrochloride; Remoxipride; Remoxipride Hydrochloride; Rimcazole Hydrochloride; Seperidol Hydrochloride; Sertindole ; Setoperone; Spiperone; Thioridazine ; Thioridazine Hydrochloride; Thiothixene; Thiothixene Hydrochloride; Tioperidone Hydrochloride; Tiospirone Hydrochloride; Trifluoperazine Hydroehloride; Trifluperidol; Triflupromazine; Triflupromazine Hydrochloride; Ziprasidone Hydrochloride.

Antirheumatic: Auranofin; Aurothioglucose; Bindarit; Lobenzarit Sodium; Phenylbutazone; Pirazolac; Prinomide Tromethamine; Seprilose.

Antischistosomal: Becanthone Hydrochloride; Hycanthone; Lucanthone Hydrochloride; Niridazole; Oxamniquine; Pararosaniline Pamoate; Teroxalene Hydrochloride.

Antiseborrheic: Chloroxine; Piroctone; Piroctone Olamine; Resorcinol Monoacetate.

Antisecretory: Arbaprostil; Deprostil; Fenoctimine Sulfate; Octreotide; Octreotide Acetate; Omeprazole Sodium; Rioprostil; Trimoprostil.

Antispasmodic: Stilonium Iodide; Tizanidine Hydrochloride.

Antithrombotic: Anagrelide Hydrochloride; Bivalirudin ; Dalteparin Sodium ; Danaparoid Sodium; Dazoxiben Hydrochloride; Efegatran Sulfate; Enoxaparin Sodium; Ifetroban; Ifetroban Sodium; Tinzaparin Sodium ; Trifenagrel.

Antitussive: Benzonatate; Butamirate Citrate; Chlophedianol Hydrochloride; Codeine Polistirex; Codoxime; Dextromethorphan; Dextromethorphan Hydrobromide; Dextromethorphan Polistirex; Ethyl Dibunate; Guaiapate; Hydrocodone Bitartrate; Hydrocodone Polistirex; Levopropoxyphene Napsylate; Noscapine; Pemcrid Nitrate; Pipazethate; Suxemerid Sulfate.

Anti-ulcerative: Aceglutamide Aluminum; Cadexomer Iodine ; Cetraxate Hydrochloride; Enisoprost; Isotiquimide; Lansoprazole; Lavoltidine Succinate; Misoprostol; Nizatidine; Nolinium Bromide ; Pantoprazole; Pifarnine; Pirenzepine Hydrochloride; Rabeprazole Sodium ; Remiprostol; Roxatidine Acetate Hydrochloride; Sucralfate; Sucrosofate Potassium; Tolimidone.

Anti-urolithic: Cysteamine; Cysteamine Hydrochloride; Tricitrates .

Antiviral: Acemannan; Acyclovir; Acyclovir Sodium; Adefovir; Alovudine; Alvircept Sudotox; Amantadine Hydrochloride; Aranotin; Arildone; Atevirdine Mesylate; Avridine; Cidofovir; Cipamfylline; Cytarabine Hydrochloride; Delavirdine Mesylate; Desciclovir; Didanosine; Disoxaril; Edoxudine; Enviradene; Enviroxime; Famciclovir; Famotine Hydrochloride; Fiacitabine; Fialuridine; Fosarilate; Foscarnet Sodium; Fosfonet Sodium; Ganciclovir; Ganciclovir Sodium; Idoxuridine; Kethoxal; Lamivudine; Lobucavir; Memotine Hydrochloride; Methisazone; Nevirapine; Penciclovir; Pirodavir; Ribavirin; Rimantadine Hydrochloride; Saquinavir Mesylate; Somantadine Hydrochloride; Sorivudine; Statolon; Stavudine; Tilorone Hydrochloride; Trifluridine; Valacyclovir Hydrochloride; Vidarabine; Vidarabine Phosphate; Vidarabine Sodium Phosphate; Viroxime; Zalcitabine; Zidovudine; Zinviroxime.

Appetite suppressant: Dexfenfluramine Hydrochloride; Phendimetrazine Tartrate; Phentermine Hydrochloride.

Benign prostatic hyperplasia therapy agent: Tamsulosin Hydrochloride.

Blood glucose regulators: Human insulin; Glucagon; Tolazamide; Tolbutamide; Chloropropamide; Acetohexamide and Glipizide.

Bone resorption inhibitor: Alendronate Sodium; Etidronate Disodium; Pamidronate Disodium.

Bronchodilator: Albuterol; Albuterol Sulfate; Azanator Maleate; Bamifylline Hydrochloride; Bitolterol Mesylate; Butaprost; Carbuterol Hydrochloride; Clorprenaline Hydrochloride; Colterol Mesylate; Doxaprost; Doxofylline; Dyphylline; Enprofylline; Ephedrine; Ephedrine Hydrochloride; Fenoterol; Fenprinast Hydrochloride; Guaithylline; Hexoprenaline Sulfate ; Hoquizil Hydrochloride; Ipratropium Bromide; Isoetharine; Isoetharine Hydrochloride; Isoetharine Mesylate; Isoproterenol Hydrochloride; Isoproterenol Sulfate; Metaproterenol Polistirex; Metaproterenol Sulfate; Nisbuterol Mesylate; Oxtriphylline; Picumeterol Fumarate; Piquizil Hydrochloride; Pirbuterol Acetate; Pirbuterol Hydrochloride; Procaterol Hydrochloride; Pseudoephedrine Sulfate; Quazodine ; Quinterenol Sulfate; Racepinephrine; Racepinephrine Hydrochloride; Reproterol Hydrochloride; Rimiterol Hydrobromide; Salmeterol; Salmeterol Xinafoate; Soterenol Hydrochloride; Sulfonterol Hydrochloride; Suloxifen Oxalate; Terbutaline Sulfate; Theophylline; Xanoxate Sodium; Zindotrine; Zinterol Hydrochloride.

Carbonic anhydrase inhibitor: Acetazolamide; Acetazolamide Sodium; Dichlorphenamide; Dorzolamide Hydrochloride; Methazolamide; Sezolamide Hydrochloride.

Cardiac depressant: Acecainide Hydrochloride; Acetylcholine Chloride; Actisomide; Adenosine; Amiodarone; Aprindine; Aprindine Hydrochloride; Artilide Fumarate; Azimilide Dihydrochloride; Bidisomide; Bucainide Maleate; Bucromarone; Butoprozine Hydrochloride ; Capobenate Sodium; Capobenic Acid; Cifenline; Cifenline Succinate; Clofilium Phosphate; Disobutamide; Disopyramide; Disopyramide Phosphate; Dofetilide; Drobuline; Edifolone Acetate; Emilium Tosylate; Encainide Hydrochloride; Flecainide Acetate; Ibutilide Fumarate; Indecainide Hydrochloride; Ipazilide Fumarate; Lorajmine Hydrochloride; Lorcainide Hydrochloride; Meobentine Sulfate; Mexiletine Hydrochloride; Modecainide; Moricizine; Oxiramide; Pirmenol Hydrochloride; Pirolazamide; Pranolium Chloride; Procainamide Hydrochloride; Propafenone Hydrochloride; Pyrinoline; Quindonium Bromide; Quinidine Gluconate; Quinidine Sulfate; Recainam Hydrochloride; Recainam

Tosylate; Risotilide Hydrochloride; Ropitoin Hydrochloride; Sematilide Hydrochloride; Suricainide Maleate; Tocainide; Tocainide Hydrochloride; Transcainide.

Cardioprotectant: Dexrazoxane; Draflazine.

Cardiotonic: Actodigin; Amrinone; Bemoradan; Butopamine; Carbazeran; Carsatrin Succinate; Deslanoside; Digitalis; Digitoxin; Digoxin; Dobutamine; Dobutamine Hydrochloride; Dobutamine Lactobionate; Dobutamine Tartrate; Enoximone; Imazodan Hydrochloride; Indolidan; Isomazole Hydrochloride; Levdobutamine Lactobionate; Lixazinone Sulfate; Medorinone; Milrinone; Pelrinone Hydrochloride; Pimobendan; Piroximone; Prinoxodan; Proscillaridin; Quazinone; Tazolol Hydrochloride; Vesnarinone.

Cardiovascular agent: Dopexamine; Dopexamine Hydrochloride.

Choleretic: Dehydrocholic Acid; Fencibutirol; Hymecromone; Piprozolin; Sincalide; Tocamphyl.

Cholinergic: Aceclidine; Bethanechol Chloride; Carbachol; Demecarium Bromide; Dexpanthenol; Echothiophate Iodide; Isoflurophate; Methacholine Chloride; Neostigmine Bromide; Neostigmine Methylsulfate; Physostigmine; Physostigmine Salicylate; Physostigmine Sulfate; Pilocarpine ; Pilocarpine Hydrochloride; Pilocarpine Nitrate; Pyridostigmine Bromide.

Cholinergic agonist: Xanomeline; Xanomeline Tartrate.

Cholinesterase Deactivator: Obidoxime Chloride; Pralidoxime Chloride; Pralidoxime Iodide; Pralidoxime Mesylate.

Coccidiostat: Arprinocid; Narasin ; Semduramicin; Semduramicin Sodium.

Cognition adjuvant: Ergoloid Mesylates; Piracetam; Pramiracetam Hydrochloride; Pramiracetam Sulfate; Tacrine Hydrochloride.

Cognition enhancer: Besipirdine Hydrochloride; Linopirdine; Sibopirdine .

Gastric Acid Suppressasnt: Omeprazole.

Diagnostic aid: Aminohippurate Sodium; Anazolene Sodium; Arclofenin; Arginine ; Bentiromide; Benzylpenicilloyl Polylysine; Butedronate Tetrasodium; Butilfenin; Coccidioidin; Corticorelin Ovinc Triflutate ; Corticotropin, Repository ; Corticotropin Zinc Hydroxide; Diatrizoate Meglumine; Diatrizoate Sodium; Diatrizoic Acid; Diphtheria Toxin for Schick Test; Disofenin; Edrophonium Chloride; Ethiodized Oil; Etifenin; Exametazime; Ferristenc; Ferumoxidcs; Ferumoxsil; Fluorescein; Fluorescein Sodium; Gadobenate Dimeglumine; Gadoteridol; Gadodiamide; Gadopentetate Dimegiumine; Gadoversetamide; Histoplasmin; Impromidine Hydrochloride; Indigotindisulfonate Sodium; Indocyanine Green ; Iobenguane Sulfate I 123; Iobenzamic Acid; Iocarmate Meglumine; Iocarmic Acid; Iocctamic Acid; Iodamide; Iodamide Megiuminc; Iodipamide Mcglumine; Iodixanol; Iodoxamate Meglumine; Iodoxamic Acid; Ioglicic Acid; Ioglucol; Ioglucomide; Ioglycamic Acid; Iogulamide; Iohexol; Iomeprol; Iopamidol; Iopanoic Acid; Iopentol; Iophendylate; Iprofenin; Iopronic Acid; Ioprocemic Acid; Iopydol; Iopydone; Iosefamic Acid; Ioseric Acid; Iosulamide Meglumine; Iosumetic Acid; Iotasul; Iotetric Acid; Iothalamate Meglumine; Iothalamate Sodium; Iothalamic Acid; Iotrolan; Iotroxic Acid; Ioversol; Ioxaglate Meglumine; Ioxagiate Sodium; Ioxaglic Acid; Ioxilan; Ioxotrizoic Acid; Ipodate Calcium; Ipodate Sodium; Isosulfan Blue; Leukocyte Typing Serum; Lidofenin; Mebrofenin; Meglumine; Metrizamide; Metrizoate Sodium; Metyrapone; Metyrapone Tartrate; Mumps Skin Test Antigen; Pentetic Acid; Propyliodone; Quinaldine Blue; Schick Test Control; Sermorelin Acetate ; Sodium Iodide I 123; Sprodiamide; Stannous Pyrophosphate; Stannous Sulfur Colloid; Succimer; Teriparatide Acetate; Tetrofosmin; Tolbutamide Sodium; Tuberculin; Tyropanoate Sodium; Xylose.

Diuretic: Ambuphylline ; Ambuside; Amiloride Hydrochloride; Azolimine; Azosemide; Brocrinat; Bumetanide; Chlorothiazide; Chlorthalidone; Clazolimine; Clorexolone; Ethacrynate Sodium; Ethacrynic Acid; Etozolin; Fenquizone; Furosemide; Hydrochlorothiazide; Isosorbide; Mannitol ; Mefruside; Ozolinone; Piretanide; Spiroxasone; Torsemide; Triamterene; Triflocin; Urea.

Dopaminergic agent: Ibopamine.

Ectoparasiticidc: Nifluridide; Permethrin.

Emetic: Apomorphine Hydrochloride.

Enzyme inhibitor: Acetohydroxamic Acid; Alrestatin Sodium; Aprotinin; Benazepril Hydrochloride; Benazeprilat; Benurestat; Bromocriptine; Bromocriptine Mesylate; Cilastatin Sodium; Flurofamide; Lergotrile; Lergotrile Mesylate; Leveyeloserine; Libenzapril; Pentopril; Pepstatin; Perindopril; Polignate Sodium; Sodium Amylosulfate; Sorbinil; Spirapril Hydroehloride; Spiraprilat; Taleranol; Teprotide; Tolfamide; Zofenopril Calcium.

Estrogen: Chlorotrianisene; Dienestrol; Diethylstilbestrol; Diethylstilbestrol Diphosphate; Equilin; Estradiol; Estradiol Cypionate; Estradiol Enanthate; Estradiol Undecylate; Estradiol Valerate; Estrazinol Hydrobromide; Estriol; Estrofurate; Estrogens, Conjugated; Estrogens, Esterified; Estrone; Estropipate; Ethinyl Estradiol; Fenestrel; Mestranol; Nylestriol; Quinestrol.

Fibrinolytie: Anistreplase; Bisobrin Laetate; Brinolase.

Free oxygen radical scavenger: Pegorgotein.

Gastrointestinal Motility agents: Cisapride (Propulsid); Metoclopramide (Reglan); Hyoscyamine (Levsin).

Glucocorticoid: Amcinonide; Beclomethasone Dipropionate; Betamethasone; Betamethasone Acetate; Betamethasone Benzoate; Betamethasone Dipropionate; Betamethasone Sodium Phosphate; Betamethasone Valerate; Carbenoxolone Sodium; Clocortolone Acetate; Clocortolone Pivalate; Cloprednol; Corticotropin; Corticotropin, Repository; Corticotropin Zinc Hydroxide; Cortisone Acetate; Cortivazol; Descinolone Acetonide; Dexamethasone; Dexamethasone Sodium Phosphate; Diflucortolone; Diflucortolone Pivalate; Flucloronide; Flumethasone; Flumethasone Pivalate; Flunisolide; Fluoeinolone Aeetonide; Fluocinonide; Fluoeortolone; Fluoeortolone Caproate; Fluorometholone; Fluperolone Acetate; Fluprednisolone; Fluprednisolone Valerate; Flurandrenolide; Formocortal; Hydrocortisone; Hydrocortisone Aeetate; Hydroeortisone Buteprate; Hydroeortisone Butyrate; Hydrocortisone Sodium Phosphate; Hydrocortisone Sodium Succinate; Hydroeortisone Valerate; Medrysone; Methylprednisolone; Methylprednisolone Acetate; Methylprednisolone Sodium Phosphate; Methylprednisolone Sodium Succinate; Nivazol; Paramethasone Acetate;

Prednicarbate; Prednisolone; Prednisolone Acetate; Prednisolone Hemisuccinate; Prednisolone Sodium Phosphate; Prednisolone Sodium Succinate; Prednisolone Tebutate; Prednisone; Prednival; Ticabesone Propionate; Tralonide; Triamcinolone; Triamcinolone Acetonide; Triamcinolone Acetonide Sodium; Triamcinolone Diacetate; Triamcinolone Hexacetonide.

Gonad-stimulating principle: Buserelin Acetate; Clomiphene Citrate; Ganirelix Acetate; Gonadorelin Acetate; Gonadorelin Hydrochloride; Gonadotropin, Chorionic; Menotropins.

Hair growth stimulant: Minoxidil .

Hemostatic: Aminocaproic Acid; Oxamarin Hydrochloride; Sulmarin; Thrombin; Tranexamic Acid.

Histamine H2 receptor antagonists: Ranitidine (Zantac); Famotidine (Pepcid); Cimetidine (Tagamet); Nizatidine (Axid).

Hormone: Diethylstilbestrol; Progesterone; 17 hydroxy progesterone; Medroxyprogesterone; Norgestrel; Norethynodrel; Estradiol; Megestrol (Megace); Norethindrone; Levonorgestrel; Ethyndiol; Ethinyl estradiol; Mestranol; Estrone; Equilin; 17 alpha dihydroequilin; equilenin; 17 alpha dihydroequilenin; 17 alpha estradiol; 17 beta estradiol; Leuprolide (lupron); Glucagon; Testolactone; Clomiphene; Han menopausal gonadotropins; Human chorionic gonadotropin; Urofollitropin; Bromocriptine; Gonadorelin; Luteinizing hormone releasing hormone and analogs; Gonadotropins; Danazol; Testosterone; Dehydroepiandrosterone; Androstenedione; Dihydroestosterone; Relaxin; Oxytocin; Vasopressin; Folliculostatin; Follicle regulatory protein; Gonadoctrinins; Oocyte maturation inhibitor; Insulin growth factor; Follicle Stimulating Hormone; Lutcinizing hormone; Tamoxifen.; Corticorelin Ovine Triflutate; Cosyntropin; Metogest; Pituitary, Posterior; Seractide Acetate; Somalapor; Somatrem; Somatropin; Somenopor; Somidobove.

Hypocholesterolemic: Lifibrol.

Hypoglycemic: Darglitazone Sodium: Glimepiride.

Hypolipidemic: Azalanstat Dihydrochloride; Colestolone; Surfomer; Xenalipin.

Hypotensive: Viprostol.

HMGCoA reductase inhibitors: Lovastatin (Mevacor); Simvastatin (Zocor); Pravastatin (Pravachol); Fluvasatin (Lescol).

Immunizing agent: Antirabies Serum; Antivenin (Latrodectus mactans); Antivenin (Micrurus Fulvius); Antivenin (Crotalidae) Polyvalent; BCG Vaccine; Botulism Antitoxin; Cholera Vaccine; Diphtheria Antitoxin; Diphtheria Toxoid; Diphtheria Toxoid Adsorbed; Globulin, Immune; Hepatitis B Immune Globulin; Hepatitis B Virus Vaccine Inactivated; Influenza Virus Vaccine; Measles Virus Vaccine Live; Meningococcal Polysaccharide Vaccine Group A; Meningococcal Polysaccharide Vaccine Group C; Mumps Virus Vaccine Live; Pertussis Immune Globulin; Pertussis Vaccine; Pertussis Vaccine Adsorbed; Plague Vaccine; Poliovirus Vaccine Inactivated; Poliovirus Vaccine Live Oral; Rabies Immune Globulin; Rabies Vaccine; Rh_0(D) Immune Globulin; Rubella Virus Vaccine Live; Smallpox Vaccine; Tetanus Antitoxin; Tetanus Immune Globulin; Tetanus Toxoid; Tetanus Toxoid Adsorbed; Typhoid Vaccine; Yellow Fever vaccine; Vaccinia Immune Globulin; Varicella-Zoster Immune Globulin.

Immunomodulator: Dimepranol Acedoben; Imiquimod; Interferon Beta-1b; Lisofylline; Mycophenolate Mofetil; Prezatide Copper Acetate.

Immunoregulator: Azarole; Fanetizole Mesylate; Frentizole; Oxamisole Hydrochloride; Ristianol Phosphate; Thymopentin; Tilomisole.

Immunostimulant: Loxoribine ; Teceleukin.

Immunosuppressant: Azathioprine; Azathioprine Sodium; Cyclosporine; Daltroban; Gusperimus Trihydrochloride; Prednisolone Sodium Phosphate, Prednisolone; Sirolimus; Tacrolimus.

Impotence therapy adjunct: Delequamine Hydrochloride.

Inhibitor: Acarbose; Atorvastatin Calcium; Benserazide ; Brocresine; Carbidopa; Clavulanate Potassium; Dazmegrel; Docebenone; Epoprostenol; Epoprostenol Sodium; Epristeride; Finasteride;

Flurbiprofen Sodium; Furegrelate Sodium; Lufironil; Miglitol; Orlistat; Pimagedine Hydrochloride; Pirmagrel; Ponalrestat; Ridogrel; Sulbactam Benzathine ; Sulbactam Pivoxil ; Sulbactam Sodium ; Suronacrine Maleate; Tazobactam; Tazobactam Sodium; Ticlopidine Hydrochloride; Tirilazad Mesylate; Tolrestat; Velnacrine Maleate; Zifrosilone; Zileuton.

Keratolytic: Aleloxa ; Aldioxa ; Benzoyl Peroxide; Dibenzothiophene; Etarotene; Isotretinoin; Motretinide; Picotrin Diolamine; Resorcinol; Resorcinol Monoacetate ; Salicylic Acid; Sumarotene; Tazarotene; Tetroquinone; Tretinoin.

LHRH agonist: Deslorelin; Goserelin; Histrelin; Lutrelin Acetate; Nafarelin Acetate.

Liver disorder treatment: Malotilate.

Luteolysin: Fenprostalene.

Memory adjuvant: Dimoxamine Hydrochloride; Ribaminol.

Mental performance enhancer: Aniracetam.

Mood regulator: Fengabine.

Mucolytic: Acetylcysteine; Carbocysteine; Domiodol.

Mucosal Protective agents: Misoprostol (Cytotec).

Mydriatic: Berefrine.

Nasal decongestant: Nemazoline Hydrochloride; Pseudoephedrine Polistirex.

Neuroleptic: Duoperone Fumarate; Risperidone.

Neuromuscular blocking agent: Atracurium Besylate; Cisatracurium Besylate; Doxacurium Chloride; Gallamine Triethiodide; Metocurine Iodide; Mivacurium Chloride; Pancuronium Bromide; Pipecuronium Bromide; Rocuronium Bromide; Succinylcholine Chloride; Tubocurarine Chloride; Vecuronium Bromide.

Neuroprotective: Dizocilpine Maleate.

NMDA antagonist: Selfotel.

Non-hormonal sterol derivative: Pregnenolone Succinate.

Oxytocic: Carboprost; Carboprost Methyl; Carboprost Tromethamine; Dinoprost ; Dinoprost Tromethamine ; Dinoprostone ; Ergonovine Maleate; Metenoprost ; Methylergonovine Maleate; Oxytocin; Sparteine Sulfate.

Plasminogen activator: Alteplase; Urokinase.

Platelet activating factor antagonist: Lexipafant.

Platelet aggregation inhibitor: Acadesine; Beraprost; Beraprost Sodium; Ciprostene Calcium; Itazigrel; Lifarizine; Oxagrelate.

Post-stroke and post-head trauma treatment: Citicoline Sodium.

Potentiator: Pentostatin; Talopram Hydrochloride.

Progestin: Algestone Acetophenide; Amadinone Acetate; Anagestone Acetate; Chlormadinone Acetate; Cingestol; Clogestone Acetate; Clomegestone Acetate; Desogestrel; Dimethisterone; Dydrogesterone; Ethynerone; Ethynodiol Diacetate; Etonogestrel; Flurogestone Acetate; Gestaclone; Gestodene; Gestonorone Caproate; Gestrinone; Haloprogesterone; Hydroxyprogesterone Caproate; Levonorgestrel; Lynestrenol; Medrogestone; Medroxyprogesterone Acetate; Methynodiol Diacetate;

Norethindrone; Norethindrone Acetate; Norethynodrel; Norgestimate; Norgestomet; Norgestrel; Oxogestone Phenpropionate; Progesterone; Quingestanol Acetate; Quingestrone; Tigestol.

Prostaglandin: Cloprostenol Sodium; Fluprostenol Sodium; Gemeprost; Prostalene; Sulprostone.

Prostate growth inhibitor: Pentomone.

Prothyrotropin: Protirelin.

Psychotropic: Minaprine.

Pulmonary surface: Beractant; Colfosceril Palmitate.

Radioactive agent: Fibrinogen I 125 ; Fludeoxyglucose F 18 ; Fluorodopa F 18 ; Insulin I 125; Insulin I 131; Iobenguane I 123; Iodipamide Sodium I 131 ; Iodoantipyrine I 131 ; Iodocholesterol I 131 ; Iodohippurate Sodium I 123 ; Iodohippurate Sodium I 125 ; Iodohippurate Sodium I 131 ; Iodopyracet I 125 ; Iodopyracet I 131 ; Iofetamine Hydrochloride I 123 ; Iomethin I 125 ; Iomethin I 131 ; Iothalamate Sodium I 125 ; Iothalamate Sodium I 131 ; Iotyrosine I 131; Liothyronine I 125; Liothyronine I 131; Merisoprol Acetate Hg 197; Merisoprol Acetate Hg 203; Merisoprol Hg 197 ; Selenomethionine Se 75 ; Technetium Tc 99m Antimony Trisulfide Colloid; Technetium Tc 99m Bicisate ; Technetium Tc 99m Disofenin ; Technetium Tc 99m Etidronate ; Technetium Tc 99m Exametazime ; Technetium Tc 99m Furifosmin ; Technetium Tc 99m Gluceptate ; Technetium Tc 99m Lidofenin ; Technetium Tc 99m Mebrofenin ; Technetium Tc 99m Medronate ; Technetium Tc 99m Medronate Disodium; Technetium Tc 99m Mertiatide ; Technetium Tc 99m Oxidronate ; Technetium Tc 99m Pentetate; Technetium Tc 99m Pentetate Calcium Trisodium; Technetium Tc 99m Sestamibi ; Technetium Tc 99m Siboroxime ; Technetium Tc 99m Succimer ; Technetium Tc 99m Sulfur Colloid ; Technetium Tc 99m Teboroxime ; Technetium Tc 99m Tetrofosmin ; Technetium Tc 99m Tiatide; Thyroxine I 125; Thyroxine I 131; Tolpovidone I 131 ; Triolein I 125; Triolein I 131.

Regulator: Calcifediol; Calcitonin; Calcitriol; Clodronic Acid; Dihydrotachysterol; Etidronic Acid; Oxidronic Acid; Piridronate Sodium; Risedronate Sodium; Secalciferol.

Relaxant: Adiphenine Hydrochloride; Alcuronium Chloride; Aminophylline; Azumolene Sodium; Baclofen; Benzoctamine Hydrochloride; Carisoprodol; Chlorphenesin Carbamate; Chlorzoxazone; Cinflumide; Cinnamedrine; Clodanolene; Cyclobenzaprine Hydrochloride; Dantrolene; Dantrolene Sodium; Fenalamide; Fenyripol Hydrochloride; Fetoxylate Hydrochloride; Flavoxate Hydrochloride; Fletazepam; Flumetramide; Flurazepam Hydrochloride; Hexafluorenium Bromide; Isomylamine Hydrochloride; Lorbamate; Mebeverine Hydrochloride; Mesuprine Hydrochloride ; Metaxalone; Methocarbamol; Methixene Hydrochloride; Nafomine Malate; Nelezaprine Maleate; Papaverine Hydrochloride; Pipoxolan Hydrochloride; Quinctolate; Ritodrine; Ritodrine Hydrochloride; Rolodine; Theophylline Sodium Glycinate; Thiphenamil Hydrochloride; Xilobam.

Repartitioning agent: Cimaterol.

Scabicide: Amitraz; Crotamiton.

Sclerosing agent: Ethanolamine Oleate; Morrhuate Sodium; Tribenoside.

Sedative: Propiomazine.

Sedative-hypnotic: Allobarbital; Alonimid; Alprazolam; Amobarbital Sodium; Bentazepam; Brotizolam; Butabarbital; Butabarbital Sodium; Butalbital; Capuride; Carbocloral; Chloral Betaine; Chloral Hydrate; Chlordiazepoxide Hydrochloride; Cloperidone Hydrochloride; Clorethate; Cyprazepam; Dexclamol Hydrochloride; Diazepam; Dichloralphenazone; Estazolam; Ethchlorvynol; Etomidate; Fenobam; Flunitrazepam; Fosazepam; Glutethimide; Halazepam; Lormetazepam; Mecloqualone; Meprobamate; Methaqualone; Midaflur; Paraldehyde; Pentobarbital; Pentobarbital Sodium; Perlapine; Prazepam; Quazepam; Reclazepam; Rolctamide; Secobarbital; Secobarbital Sodium; Suproclone; Thalidomide; Tracazolate; Trepipam Maleate; Triazolam; Tricetamide; Triclofos Sodium; Trimetozine; Uldazepam; Zaleplon; Zolazepam Hydrochloride; Zolpidem Tartrate.

Selective adenosine A1 antagonist: Apaxifylline.

Serotonin antagonist: Altanserin Tartrate; Amesergide; Ketanserin; Ritanserin.

Serotonin inhibitor: Cinanserin Hydrochloride; Fenclonine; Fonazine Mesylate; Xylamidine Tosylate.

Serotonin receptor antagonist: Tropanserin Hydrochloride.

Steroid: Dexamethasone Acefurate; Mometasone Furoate.

Stimulant: Amfonelic Acid; Amphetamine Sulfate; Ampyzine Sulfate; Arbutamine Hydrochloride; Azabon; Caffeine; Ceruletide; Ceruletide Diethylamine; Cisapride; Dazopride Fumarate; Dextroamphetamine; Dextroamphetamine Sulfate; Difluanine Hydrochloride; Dimefline Hydrochloride; Doxapram Hydrochloride; Etryptamine Acetate; Ethamivan; Fenethylline Hydrochloride; Flubanilate Hydrochloride; Flurothyl; Histamine Phosphate; Indriline Hydrochloride; Mefexamide; Methamphetamine Hydrochloride; Methylphenidate Hydrochloride; Pemoline; Pyrovalerone Hydrochloride; Xamoterol; Xamoterol Fumarate.

Suppressant: Amflutizole; Colchicine; Tazofelone.

Symptomatic multiple sclerosis: Fampridine.

Synergist: Proadifen Hydrochloride.

Thyroid hormone: Levothyroxine Sodium; Liothyronine Sodium; Liotrix.

Thyroid inhibitor: Methimazole; Propylthiouracil.

Thyromimetic: Thyromedan Hydrochloride.

Tranquilizer: Bromazepam; Buspirone Hydrochloride; Chlordiazepoxide; Clazolam; Clobazam; Clorazepate Dipotassium; Clorazepate Monopotassium; Demoxepam; Dexmedetomidine; Enciprazine Hydrochloride; Gepirone Hydrochloride; Hydroxyphenamate; Hydroxyzine Hydrochloride; Hydroxyzine Pamoate; Ketazolam; Lorazepam; Lorzafone; Loxapine; Loxapine

Succinate; Medazepam Hydrochloride; Nabilone; Nisobamate ; Oxazepam; Pentabamate; Pirenperone; Ripazepam; Rolipram; Sulazepam; Taciamine Hydrochloride; Temazepam; Triflubazam; Tybamate; Valnoctamide.

Amyotrophic lateral sclerosis agents: Riluzole.

Cerebral ischemia agents: Dextrorphan Hydrochloride.

Paget's disease agents: Tiludronate Disodium.

Unstable angina agents: Tirofiban Hydrochloride.

Uricosuric: Benzbromarone; Irtemazole; Probenecid; Sulfinpyrazone.

Vasoconstrictor : Angiotensin Amide; Felypressin; Methysergide; Methysergide Maleate.

Vasodilator: Alprostadil; Azaclorzine Hydrochloride; Bamethan Sulfate; Bepridil Hydrochloride; Buterizine; Cetiedil Citrate; Chromonar Hydrochloride; Clonitrate; Diltiazem Hydrochloride; Dipyridamole; Droprenilamine; Erythrityl Tetranitrate; Felodipine; Flunarizine Hydrochloride; Fostedil; Hexobendine; Inositol Niacinate; Iproxamine Hydrochloride; Isosorbide Dinitrate; Isosorbide Mononitrate; Isoxsuprine Hydrochloride; Lidoflazine; Mefenidil; Mefenidil Fumarate; Mibefradil Dihydrochloride; Mioflazine Hydrochloride; Mixidine; Nafronyl Oxalate; Nicardipine Hydrochloride; Nicergoline; Nicorandil; Nicotinyl Alcohol; Nifedipine; Nimodipine; Nisoldipine; Oxfenicine; Oxprenolol Hydrochloride; Pentaerythritol Tetranitrate; Pentoxifylline; Pentrinitrol; Perhexiline Maleate; Pindolol; Pirsidomine; Prenylamine; Propatyl Nitrate; Suloctidil; Terodiline Hydrochloride; Tipropidil Hydrochloride; Tolazoline Hydrochloride; Xanthinol Niacinate.

Vulnerary: Allantoin.

Wound healing agent: Ersofermin.

Xanthine oxidase inhibitor: Allopurinol; Oxypurinol

Other pharmaceutical agents include: 1-decpyrrolidinone; 1-dodecpyrrolidinone; 16-alpha fluoroestradiol; 16-epiestriol; 16alpha-gitoxin; 17alpha estradiol; 17beta estradiol; 1alpha-hydroxyvitamin D2; 2'-nor-cGMP; 20-epi-1,25 dihydroxyvitamin D3; 22-oxacalcitriol; 2CVV; 3-isobutyl GABA; 6-FUDCA; 7-methoxytacrine; abamectin; abanoquil; abecarnil; abiraterone; acadesine; acamprosate; acarbose; aceclofenac; acemannan; acetomeprogenol; acetyl-L-carnitine; acetylcysteine, N-; acetylmethadol; aeifran; acipimox; acitemate; acitretin; aclarubicin; aclatonium; napadisilate; aconiazide; acrivastinet; adafenoxate; adapalene; adatanserin; adecypenol; adefovir dipivoxil; adelmidrol; ademetionine; adinazolam; adiposin; adozelesin; adrafinil; alacepril; aladapcin; alaptide; albendazole; albolabrin; aldecalmycin; aldesleukin; alendronic acid; alentemol; alfacalcidol; alfuzosin; alglucerase; alinastine; alosetron; alpha idosone; alprostadil; altretamine; altromycin B; ambamustine; amelometasone; amesergide; amezinium metilsulfate; amfebutamone; amidox; amifloxacin; amifostine; amiodarone; amisulpride; amlexanox; amlodipine; amlodipine; ampiroxicam; amrinone; amrubicin; amsacrine; amylin; amythiamicin; anagrelide; anakinra; ananain; anaritide; anastrozole; andrographolide; anordrin; apadoline; apafant; apaxifylline; aphidicolin glycinate; apraclonidine; aprosulate sodium; aptiganel; apurinic acid; aranidipine; arbekacin; arbidol; arbutamine; ardeparin sodium; arecatannin B1; argatroban; aripiprazol; arotinolol; asimadoline; aspalatone; asperfuran; aspoxicillin; astemizole; asulacrine; atamestane; atenolol, S-; atevirdine; atosiban; atovaquone; atpenin B; atrimustine; atrinositol; aureobasidin A; azadirachtine; azasetron; azatyrosine; azelaic acid; azelastine; azelnidipine; azimilide; azithromycin; azosemide; aztreonam; baccatin III; bacoside A; bacoside B; bactobolamine; balazipone; balhimycin;. balofloxacin; balsalazide; bambuterol; baohuoside 1; barnidipine; basifungin; batebulast; batimastat; beauvericin; beclaplermin; becliconazole; befloxatone; belfosdil; bellenamine; benflumetol; benidipine; benzisoxazole; benzochlorins; benzoidazoxan; benzoylstaurosporine; benztropine; bepridil; beractant; beraprost; berlafenone; bertosamil; besipirdine; beta-alethine; betaclamycin B; betamipron; betaxolol; betulinic acid; bevantolol; bicalutamide; bifemelane; bimakalim; bimithil; binospirone; bioxalomycin alpha2; biriperone; bis-benzimidazole A; bis-benzimidazole B; bisantrene; bisaramil; bisaziridinylspermine; bisnafide; bisoprolol; bistramide D; bistramide K; bistratene A; boldine; bopindolol; brefeldin; breflate; brimonidine; bromfenac; bromperidol; bropirimine; bucindolol; budesonide; budipine; budotitane; bunaprolast; bunazosin; butenafine; buthionine sulfoximine; butixocort propionate; cadexomer iodine; calanolide A; calcipotriol; calphostin C; camonagrel; candesartan; candesartan cilexetil; candoxatril; candoxatrilat; capecitabine; capromab; capsaicin; captopril; carbazomycin C;

carbetocin; carbovir; carboxamide-amino-triazole; carboxyamidotriazole; carboxymethylated beta-1,3-glucan; carperitide; cartcolol; carumonam; carvedilol; carvotroline; carzelesin; castanospermine; cebaracetam; cecropin B; cefcapene pivoxil; cefdaloxime pentexil tosilate; cefdinir; cefditoren pivoxil; cefepime; cefetamet; cefetamet pivoxil; cefixime; cefluprenam; cefmetazole; cefminox; cefodizime; cefoselis; cefotetan; cefotiam; cefotiam hexetil; cefozopran; cefpimizole; cefpiramide; cefpirome; cefpodoxime proxetil; cefprozil; cefsulodin; cefteram; ceftibuten; ceftriaxone; cefuroxime axetil; celastrol; celikalim; celiprolol; cepacidine A; cericlamine; cerivastatin; ceronapril; certoparin sodium; cetiedil; cetirizine; chloroorienticin A; chloroorienticin B; chloroquinoxaline sulfonamide; cibenzoline; cicaprost; ciclesonide; cicletanine; cicloprolol; cidofovir; cilansetron; cilazapril; cilnidipine; cilobradine; cilostazol; cimetropium bromide; cinitapride; cinolazepam; cioteronel; ciprofibrate; ciprofloxacin; ciprostene; cis-porphyrin; cisapride; cisatracurium besilate; cistinexine; citalopram; citicoline; citreamicin alpha; cladribine; clarithromycin; clausenamide; clebopride; clinafloxacin; clobazam; clobetasone butyrate; clodronic acid; clomethiazole; clopidogrel; clotrimazole; colestimide; colfosceril palmitate; collismycin A; collismycin B; combretastatin A4; complestatin; conagenin; contignasterol; contortrostatin; cosalane; costatolide; cotinine; coumermycin A1; cucumariosid; curacin A; curdlan sulfate; curiosin; cyclazosin; cyclic HPMPC; cyclobenzaprine; cyclobut A; cyclobut G; cyclocapron; cycloplatam; cyclosin; cyclothialidine; cyclothiazomycin; cypemycin; cyproterone; cytarabine ocfosfate; cytochalasin B; dacliximab; dactimicin; daidzein; daidzin; dalfopristin; dalteparin sodium; danaparoid; daphnodorin A; dapiprazole; dapitant; darifenacin; darlucin A; darsidomine; ddUTP; decitabine; deferiprone; deflazacort; dehydrodidemnin B; dehydroepiandrosterone; delapril; delequamine; delfaprazine; delmopinol; delphinidin; deoxypyridinoline; deprodone; depsidomycin; derameiclane; dermatan sulfate; desflurane; desirudin; desloreiin; desmopressin; desogestrel; desoxoamiodarone; detajmium bitartrate; dexifosfamide; dexketoprofen; dexloxiglumide; dexmedetomidine; dexpemedolac; dexrazoxane; dexsotalol; dextrin 2-sulphate; dexverapamil; dezinamide; dezocine; diaziquone; diclofenac digolil; diclofenac potassium; dicranin; didemnin B; didox; dienogest; diethylhomospermine; diethylnorspermine; dihydrexidine; dihydro-5-azacytidine; dimethyl prostaglandin A1; dimethylhomospermine; dimiracetam; dioxamycin; diphencyprone; diphenyl spiromustine; diprafenone; dipropylnorspermine; dirithromycin; discodermolide; disulfiram; ditekiren; docarpamine; docosanol, 1-; dofetilide; dolasetron; domitroban; dopexamine; dorzolamide; dosmalfate; dotarizine; doxacurium chloride; doxazosin; doxifluridine; doxofylline; draculin; draflazine; droloxifene; dronabinol; drosperidone; drotaverine acephyllinate; droxicam;

ebiratide; ebrotidine; ebselen; ecabapide; ecabet; ecadotril; ecdisteron; echicetin; echistatin; ecomustine; ecteinascidin 722; ecteinascidin 729; ecteinascidin 743; edaravone; edelfosine; edobacomab; edrecolomab; efegatran; eflornithine; efonidipine; egualen; eleatonin; eletriptan; elgodipine; eliprodil; eltenac; emakalim; emedastine; emiglitate; emitefur; emoctakin; enadoline hydrochloride; enalapril; enazadrem; englitazone; enlimomab; enoxacin; enoxaparin sodium; enoximone; entacapone; enterostatin; epoprostenol; epoxymexrenone; epristeride; eprosartan; eptastigmine; erdosteine; ersentilide; ersofermin; erythritol; esuprone; etanidazole; etanterol; ethacizin; ethinylestradiol; etizolam; etodolac; etoposide phosphate; etrabamine; everninomicin; examorelin; exemestane; fadrozole; faeriefungin; famciclovir; fampridine; fantofarone; faropenem; fasidotril; fasudil; fazarabine; fedotozine; felbamate; fenofibrate; fenoldopam; fenretinide; fenspiride; fenticonazole; fepradinol; ferpifosate sodium; ferristene; ferrixan; ferumoxsil; fexofenadine; flavopiridol; flecainide; flerobuterol; fleroxacin; flesinoxan; flezelastine; flobufen; flomoxef; florfenicol; florifenine; flosatidil; fluasterone; fluconazole; fludarabine; flumazenil; flumecinol; flumequine; flunarizine; fluocalcitriol; fluorodaunorunicin hydrochloride; fluoxetine, R-; fluoxetine, S-; fluparoxan; flupirtine; flurbiprofen axetil; flurithromycin; fluticasone propionate; flutrimazole; fluvastatin; fluvoxamine; forasartan; forfenimex; formestane; formoterol; formoterol, R,R-; fosfomycin; trometamol; fosinopril; fosphenytoin; fostriecin; fotemustine; gabapentin; gadobenic acid; gadobutrol; gadodiamide; gadodiamide-EOB-DTPA; gadolinium texaphyrin; gadoteric acid; gadoteridol; gadoversetamide; galantamine; galdansetron; gallopamil; galocitabine; gamolenic acid; ganirelix; gepirone; gestrinone; girisopam; glaspimod; glaucocalyxin A; glutapyrone; glycopine; glycopril; granisetron; grepafloxacin; halichondrin B; halofantrine; halomon; halopredone; hatomamicin; hatomarubigin A; hatomarubigin B; hatomarubigin C; hatomarubigin D; ibogaine; ibopamine; ibudilast; illimaquinone; ilmofosine; ilomastat; iloperidone; iloprost; imidapril; imidazenil; indinavir; indolidan; indometacin farnesil; indometacin; tropine ester; indoramin; inocoterone; inogatran; inolimomab; interferon alfa; interferon alfa-2a; interferon alfa-2b; interferon alfa-N1; interferon alfa-n3; interferon beta; interferon beta-1al; interferon beta-1b; interferon gamma-1a; interferon gamma-1b; interferon omega; interferon, consensus; interleukin-1; interleukin-1 alpha; interleukin-1 beta; interleukin-10; interleukin-11; interleukin-12; interleukin-12; interleukin-15; interleukin-2; interleukin-3; interleukin-4; interleukin-5; interleukin-7; interleukin-8; iobenguane; iobitridol; iodoamiloride; iododoxorubicin; iofratol; iomeprol; iopentol; iopromide; iopyrol; iotriside; ioversol; ioxilan; ipazilide; IpdR; ipenoxazone; ipidacrine; ipomeanol, 4-; ipriflavone; ipsapirone; irbesartan; irinotecan; irloxacin; irsogladine; irtemazole; isalsteine; isbogrel;

isepamicin; isobengazole; isofloxythepin; isohomohalicondrin B; isopropyl unoprostone; isradipine; itameline; itasetron; itopride; itraconazole; ketoprofen, R-; ketoprofen, S-; ketorolac; lacidipine; lactitol; lactivicin; laennec; lafutidine; lamellarin-N triacetate; lamifiban; lamivudine; lamotrigine; lanoconazole; lanperisone; lanreotide; lansoprazole; latanoprost; lateritin; laurocapram; lazabemide; lemefloxacin; lemildipine; leminoprazole; lenercept; lenograstim; lentinan sulfate; leptin; leptolstatin; lercanidipine; lerisetron; lesopitron; letrazuril; letrozole; leucomyzin; leuprorelin; leveromakalim; levetiracetam; levobetaxolol; levobunolol; levobupivacaine; levocabastine; levocarnitine; levodropropizine; levofloxacin; levomoprolol; levonorgestrel; levormeloxifene; levosimendan; levosulpiride; linotroban; linsidomine; lintitript; lintopride; liothyronine sodium; lirexapride; lisinopril; lobaplatin; lobucavir; lodoxamide; lombricine; lomefloxacin; lomerizine; lometrexol; lonazolac; lonidamine; loracarbef; loratadine; lorglumide; lornoxicam; losartan; losigamone; losoxantrone; loteprednol; loviride; loxoribine; lubeluzole; lurtotecan; luteinizing hormone; lutetium; luzindole; lydicamycin; lysofylline; lysostaphin; magainin 2 amide; magnolol; mallotochromene; mallotojaponin; malotilate; mangafodipir; manidipine; maniwamycin A; mannostatin A; manumycin E; manumycin F; mapinastine; marimastat; Martek 8708; Martek 92211; masoprocol; maspin; massetolide; meterelin; methoxatone; methylhistamine, R-alpha; methylinosine monophosphate; methylprednisolone aceponate; methylprednisolone suleptanate; metipamide; metoclopramide; metoprolol, S-; metrifonate; mibefradil; michellamine B; microcolin A; midodrine; mifepristone; miglitol; milacemide; milameline; mildronate; milnacipran; milrinone; miltefosine; minaprine; miokamycin; mipragoside; mirfentanil; mirimostim; mirtazapine; misoprostol; mitoguazone; mitolactol; mitonafide; mitoxantrone; mivacurium chloride; mivazerol; mixanpril; mizolastine; mizoribine; moclobemide; modafinil; moexipril; mofarotene; mofezolac; molgramostim; mometasone; montirelin; mopidamol; moracizine; mosapramine; mosapride; motilide; moxiraprine; moxonidine; nadifloxacin; nadroparin calcium; nafadotride; nafamostat; nafarelin; naftopidil; naglivan; nagrestip; nalmefene; naphterpin; napsagatran; naratriptan; nartograstim; nasaruplase; nateplase; niperotidine; niravoline; nisamycin; nisin; nisoldipine; nitazoxanide; nitecapone; nitrendipine; nitrendipine, S-; nitrofurantoin monohydrate; nitrullyn; nizatidine; ofloxacin; okicenone; olanzapine; olopatadine; olprinone; olsalazine; omeprazole; onapristone; ondansetron; ondansetron, R-; ontazolast; oracin; otenzepad; oxaliplatin; oxamisole; oxandrolone; oxaprozin; oxaunomycin; oxcarbazepine; oxiconazole; oxiracetam; oxodipine; ozagrel; palauamine; palinavir; palmitoylrhizoxin; pamaqueside; pamicogrel; pamidronic acid; panamesine; panaxytriol; panipenem; panipenum; pannorin; panomifene; pantethine; pantoprazole; parabactin;

parnaparin sodium; paroxetine; parthenolide; pazelliptine; pazufloxacin; pefloxacin; pegaspargase; peldesine; pemedolae; pemirolast; penciclovir; pentafuside; pentamidine; pentamorphone; pentigetide; pentosan; pentostatin; pentrozole; perflubron; perfosfamide; pergolide; perindoprilat; perospirone; phenaridine; phenazinomycin; phenserine; phensuccinal; phentolamine mesilate; phenylacetate; phenylalanyl ketoconazole; picenadol; picibanil; picroliv; picumeterol; pidotimod; pilocarpine hydrochloride; pilsicainide; pimagedine; pimilprost; pimobendan; pinacidil; pinocebrin; pioglitazone; pipecuronium bromide; pirarubicin; piretanide; pirfenidone; piritrexim; pirlindole; pirmagrel; pirmenol; pirodavir; pirodomast; piroxicam cinnamate; propagermanium; propentofylline; propionylcarnitine, L-; propiram; propiram + paracetamol; propiverine; propyl bis-acridone; prostaglandin J2; prostratin; protegrin; protosufloxacin; prulifloxacin; pyrazoloacridine; quazepam; quetiapine; quiflapon; quinagolide; quinapril; quinfamide; quinupristin; raloxifene; raltitrexed; ramatroban; ramipril; ramosetron; ranelic acid; ranitidine bismuth citrate; ranolazine; recainam; regavirumab; relaxin; repirinast; resinferatoxin; reticulon; reviparin sodium; revizinone; ricasetron; ridogrel; rifabutin; rifapentine; rifaximin; rilopirox; riluzole; rimantadine; rimexolone; rimoprogin; riodipine; ripisartan; risedronic acid; rispenzepine; risperidone; ritanserin; ritipenem; ritipenem acoxil; ritolukast; ritonavir; rizatriptan benzoate; rohitukine; rokitamycin; ropinirole; ropivacaine; roquinimex; roxatidine; roxindole; roxithromycin; rubiginone B1; ruboxyl; rufloxacin; rupatidine; ruzadolane; safingol; safironil; saintopin; salbutamol, R-; salmeterol; salmeterol, R-salnacedin; sameridine; sampatrilat; sanfetrinem; saprisartan; sapropterin; saquinavir; SarCNU; sarcophytol A sargramostim; sarpogrelate; saruplase; saterinone; satigrel; satumomab pendetide; selegiline; selenium thiosemicarbazone; sematilide; semduramicin; semotiadil; semustine; sermorelin; sertaconazole; sertindole; sertraline; setiptiline; sevirumab; sevoflurane; sezolamide; silipide; silteplase; simendan; simvastatin; sinitrodil; sinnabidol; sipatrigine; sirolimus; sizofiran; somatomedin B; somatomedin C; somatrem; somatropin; sonermin; sotalol; staurosporine; stavudine; stepronin; stipiamide; stiripentol; stobadine; succibun; sucralfate; sulfasalazine; sulfinosine; sulfoxamine; sulopenem; sultamicillin; sultopride; sulukast; sumatriptan; symakalim; tandospirone; tapgen; taprostene; tasosartan; tazanolast; tazarotene; teicoplanin; telenzepine; tellurapyrylium; telmesteine; telmisartan; temoeapril; temoporfin; temozolomide; tenidap; teniposide; tenosal; tenoxicam; tepirindole; tepoxalin; terazosin; terbinafine; terfenadine; terflavoxate; terguride; terlakiren; terlipressin; terodiline; tertatolol; testosterone bucielate; tetrachlorodecaoxide; tetrazomine; thaliblastine; thalidomide; thiocoraline; thiofedrine; thiomarinol; thioperamide; thyroid stimulating hormone; tiagabine; tianeptine; tiapafant; tibolone; tielopidine;

tienoxolol; tilisolol; tilnoprofen arbamel; tiludronic acid; tinzaparin sodium; tiotropium bromide; tipredane; tiqueside; tirandalydigin; tirapazamine; tirilazad; tirofiban; tiropramide; topsentin; torasemide; toremifene; tosufloxacin; trafermin; trandolapril; traxanox; tretinoin; tretinoin tocoferil; triacetyluridine; tricaprilin; trichohyalin; trichosanthin, alpha; trieiribine; trientine; triflavin; trimegestone; triptorelin; troglitazone; trombodipine; tropisetron; trospectomycin; trovafloxacin; trovirdine; tucaresol; tulobuterol; tylogenin; urapidil; uridine triphosphate; valaeielovir; valproate magnesium; valproate semisodium; valsartan; vamicamide; vanadeine; vaninolol; vapreotide; variolin B; velaresol; venlafaxine; veramine; verapamil, (S); verdins; veroxan; verteporfin; vesnarinone; vexibinol; vigabatrin; vinburnine citrate; vinburnine resinate; vinconate; vinorelbine; vinpocetine; vinpocetine citrate; vintoperol; vinxaltine; voriconazole; vorozole; voxergolide; xemilofiban; ximoprofen; yangambin; zabicipril; zacopride; zacopride, R-; zafirlukast; zalcitabine; zaleplon; zalospirone; zaltoprofen; zanamivir; zankiren; zanoterone; zatebradine; zatosetron; zenarestat; zeniplatin; zifrosilone; zilaseorb; zileuton; zinostatin stimalamer; ziprasidone; zoledronic acid; zolmitriptan; zolpidem; zonisamide; zopiclone; zopiclone, S-; zopolrestat; zotepine.

Also included are commonly used geriatrie drugs, sueh as Furosemide, Lanoxin, Potassium Chloride, Depakote, Trazodone-HCL, Zantae, Dilantin, Zobolt, Risperdal, Prilosec, Folic Acid, Halperidol, Axid, Carbamazepine, Metoprolol Tartrate, Prinivil, Coumadin, Tegretol, Propulsid, Hydrochlorothiazide, Digoxin, Nitroglycerin, Methyldopa, Prazosin, Oral Hypoglycemics.

Particularly important agents are: amantadine hydrochloride, hyoscyamine sulfate, fluoxetine and trazodone hydrochloride for neurological disorders; nifidipine, diltiazem, phenotoxifyline for cardiovascular diseasc; ketoprofen, aspirin, piroxicam, indomethacin, ibuprofen for arthritis; omeprazole for uleers, and isotretinoin for eaneer.

Thc agent may bc a sunsereen agent. Examples of sunsercen agents inelude: p-aminobenzoate analogs sueh as 2-ethylhexyl-4-dimethylaminobenzoate (Padimate O); p-methoxy-2-ethyl-hexyl-cinnamate (Parsol 1789); oxybenzone (benzophenone-3); ethylhexylsalicylate; diphenylaerylate polyisobutylene; alkyl-β,β-diphenylacrylate and α-cyano-β,β-diphenylacrylate; 1-(4-aminophenyl)-2-morpholinylethanone;(1-(4-methoxylphenyl)-3-(4-tert-butyl-phenyl)-propan-1-3-dione; methyl anthranilate; oetoerylene; Tretinoin α-hydroxyaeid; diphenylaerylate polyisobutylene; 1-(4-aminophenyl)-2-morpholinylethanone; diphenylaerylate polyisobutylene; digalloyl trioleate; glyeeryl p- aminobenzoate; 4-(omega -dialkylaminoalkoxy)phenylmethylene)-1,3,3-trimethyl-2-oxabicyclo(2.2.2)octan-6-ones; 5-(arylmethylene)-1,3,3-trimethyl-2-oxabieyclo(2.2.2)octan-6-ones; melanin.

The agent also can be insect repellants. A widely used insect repellant is N-N-diethyl-3-methylbenzamide.

The agent also may be cultured cells, lyophillized and captured within the matrix of the flake. Such cells can be recombinant cells engineered to produce desirable therapeutic products.

Imaging agents are agents capable of imaging a desired site, e.g. tumor, in vivo. Examples of imaging agents include substances having a label which is detectable in vivo, e.g. antibodies attached to fluorescent labels. The term antibody includes whole antibodies or fragments thereof.

Specific targeting agents include agents capable of delivering a therapeutic agent to a desired site, e.g. tumor, and providing a therapeutic effect. Examples of targeting agents include agents which can carry toxins or other agents which provide beneficial effects. The targeting agents can be an antibody linked to a toxin, e.g. ricin A or an antibody linked to a drug.

Neurotransmitters are substances which are released from a neuron on excitation and travel to either inhibit or excite a target cell. Examples of neurotransmitters include dopamine, serotonin, q-aminobutyric acid, norepinephrine, histamine, acetylcholine, and epinephrine.

Cell response modifiers are chemotactic factors such as platelet-derived growth factor (PDGF). Other chemotactic factors include neutrophil-activating protein, monocyte chemoattractant protein, macrophage-inflammatory protein, platelet factor, platelet basic protein, and melanoma growth stimulating activity; epidermal growth factor, transforming growth factor (alpha), fibroblast growth factor, platelet-derived endothelial cell growth factor, insulin-like growth factor, nerve growth factor, and bone growth/cartilage-inducing factor (alpha and beta), or other bone morphogenetic protein.

Other cell response modifiers are the interleukins, interleukin inhibitors or interleukin receptors, including interleukin 1 through interleukin 10; interferons, including alpha, beta and gamma; hematopoietic factors, including erythropoietin, granulocyte colony stimulating factor, macrophage colony stimulating factor and granulocyte-macrophage colony stimulating factor; tumor necrosis factors, including alpha and beta; transforming growth factors (beta), including beta-1, beta-2, beta-3, inhibin, and activin; and bone morphogenetic proteins.

Antioxidants are substances which inhibit oxidation or suppress reactions promoted by oxygen or peroxides. Antioxidants, especially lipid-soluble antioxidants, can be absorbed into the cellular membrane to neutralize oxygen radicals and thereby protect the membrane. The antioxidants useful in the present invention may be selected from the group consisting of all forms of Vitamin A including retinal and 3,4-didehydroretinal, all forms of carotene such as Alpha-carotene, beta

-carotene (beta, beta -carotene), gamma-carotene, delta-carotene, all forms of Vitamin C (D-ascorbic acid, L-aseorbic acid), all forms of tocopherol such as Vitamin E (Alpha-tocopherol, 3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltri-decyl)-2H-1- benzopyran-6- ol), beta -tocophcrol, gamma-tocopherol, delta-tocopherol, tocoquinonc, tocotrienol, and Vitamin E esters which rcadily undergo hydrolysis to Vitamin E such as Vitamin E acetate and Vitamin E succinate, and pharmaccutically acceptablc Vitamin E salts such as Vitamin E phosphate, prodrugs of Vitamin A, carotenc, Vitamin C, and Vitamin E, pharmaccutically acceptablc salts of Vitamin A, carotenc, Vitamin C, and Vitamin E, and thc like, and mixtures thereof.

In addition to the above ingredients, there may also be incorporated other additives selected from among the various pharmaceutically acceptable additives available to those skilled in the art. These additives include binders, stabilizers, preservatives, flavorings and pigments. In some embodiments, the compositions of the present invention also contain a binder such as lecithin which "binds" the other ingredients, thereby enhancing the uniform consistency of the final composition.

When administered as flakes containing drugs, the formulations of the invention are applied in pharmaceutically acceptable amounts and in pharmaceutically acceptable compositions. Such preparations may routinely contain salts, buffering agents, preservatives, compatible carriers, and optionally other therapeutic ingredients. When used in medicine the salts should be pharmaceutically acceptable, but non-pharmaceutically acceptable salts may conveniently be used to prepare pharmaceutically acceptable salts thereof and are not excluded from the scope of the invention. Such pharmacologically and pharmaceutically acceptable salts include, but are not limited to, those prepared from the following acids: hydrochloric, hydrobromic, sulphuric, nitric, phosphoric, maleic, acetic, salicylic, p-toluene sulfonic, tartaric, citric, methane sulfonic, formic, malonic, succinic, naphthalene-2-sulfonic, and benzene sulfonic. Also, pharmaceutically acceptable salts can be prepared as alkaline metal or alkaline earth salts, such as sodium, potassium or calcium salts.

Suitable buffering agents include: acetic acid and a salt (1-2% W/V); citric acid and a salt (1-3% W/V); and phosphoric acid and a salt (0.8-2% W/V).

Suitable preservatives include benzalkonium chloride (0.003-0.03% W/V); chlorobutanol (0.3-0.9% W/V); parabens (0.01-0.25% W/V) and thimerosal (0.004-0.02% W/V).

The active compounds of the present invention may be a pharmaceutical composition having a therapeutically effective amount optionally included in a pharmaceutically-acceptable carrier. The term "pharmaceutically-acceptable carrier" as used herein means one or more compatible solid or

liquid-filler, dilutants or encapsulating substances which are suitable for administration to a human or other animal. The term "carrier" denotes an organic or inorganic ingredient, natural or synthetic, with which the active ingredient is combined to facilitate the application. The components of the pharmaceutical compositions are capable of being commingled with the flakes of the present invention, and with each other, in a manner such that there is no interaction which would substantially impair the desired pharmaceutical efficacy.

Compositions suitable for parenteral administration conveniently comprise a sterile preparation. This preparation may be formulated according to known methods. The sterile preparation thus may be a sterile solution or suspension in a non-toxic parenterally-acceptable diluent or solvent. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono or di-glycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables. Carrier formulations suitable for oral, subcutaneous, intravenous, intramuscular, etc. can be found in Remington's Pharmaceutical Sciences, Mack Publishing Company, Easton, PA.

A subject as used herein means humans, primates, horses, cows, pigs, sheep, goats, dogs, cats and rodents.

The conjugates of the invention are administered in effective amounts. An effective amount means that amount necessary to delay the onset of, inhibit the progression of, halt altogether the onset or progression of or diagnose the particular condition being treated. When administered to a subject, effective amounts will depend, of course, on the particular condition being treated; the severity of the condition; individual patient parameters including age, physical condition, size and weight; concurrent treatment; frequency of treatment; and the mode of administration. These factors are well known to those of ordinary skill in the art and can be addressed with no more than routine experimentation. It is preferred generally that a maximum dose be used, that is, the highest safe dose according to sound medical judgment.

Dosage may be adjusted appropriately to achieve desired drug levels, locally or systemically. Generally, daily oral doses of active compounds will be from about 0.01 mg/kg per day to 1000 mg/kg per day. In the event that the response in a subject is insufficient at such doses, even higher doses (or effective higher doses by a different, more localized delivery route) may be employed to the extent that patient tolerance permits.

A variety of administration routes are available. The particular mode selected will depend of course, upon the particular drug selected, the severity of the disease state being treated and the

dosage required for therapeutic efficacy. The methods of this invention, generally speaking, may be practiced using any mode of administration that is medically acceptable, meaning any mode that produces effective levels of the active compounds without causing clinically unacceptable adverse effects. Such modes of administration include oral, rectal, sublingual, topical, nasal, transdermal, intradermal or parenteral routes. The term "parenteral" includes subcutaneous, intravenous, intramuscular, or infusion. Intravenous routes are preferred.

The compositions may conveniently be presented in unit dosage form and may be prepared by any of the methods well known in the art of pharmacy. All methods include the step of bringing the conjugates of the invention into association with a carrier which constitutes one or more accessory ingredients. In general, the compositions are prepared by uniformly and intimately bringing the compounds into association with a liquid carrier, a finely divided solid carrier, or both, and then, if necessary, shaping the product.

Compositions suitable for oral administration may be presented as discrete units such as capsules, cachets, tablets, or lozenges, each containing a predetermined amount of the active compound. Other compositions include suspensions in aqueous liquors or non-aqueous liquids such as a syrup, an elixir, or an emulsion.

Examples

Drug-Incorporated Flakes (DIF)

A. Spray drying method

A drug solution containing acceptable pharmaceutical excipient is sprayed onto a rotating drum (roll drum drier). The system can be warm and under reduced pressure, depending on the drug and solution characteristics. The thickness of the flake is determined by the rate of drum roation rate, temperature, partial pressure, humidity, and composition of the drug solution.

The drug flakes are reduced to the desired size (1 um to 5 mm) by a mechanical mill. The preferred range is 10-500 um.

The flakes are fractionated to the desired size distribution using mechanical screens or used as is.

The desired fractions are coated with a single or more coatings comprised of natural or synthetic polymers using a spray coater. The first coat can be comprised of methyl cellulose while the second can be a synthetic ionic polymer to impart selective solubility to the coating.

B. Roll Milling

Using acceptable pharmaceutical processing methods a drug substance is formulated and granulated.

The granules are compressed between a rolling mechanism including at least one deflection-compensating roller. Flakes are formed of a thickness of less than 0.1 mm.

The flakes are dried and processed as above.

C. Thin-film Manufacturing

Onto a moving belt is sprayed a thin film of coating agent such as ethyl cellulose. After drying a drug solution contained in a non-miscible solvent for the coating layer is sprayed. After drying a second layer of coating solution is sprayed to for a 3-laminated product.

The product is removed with a fixed knife blade and milled to form uniform flakes by mechanical milling. The preferred size range is 100-500 um.

The flakes are coated again to cover the edges and/or to add additional desired properties such as to provide a slip, taste masking or a moisture barrier or sustained or controlled release characteristic.

D. Spray, Inkjet or Drip Method

1. Inkjet, spray, or drip drug slurry onto belt dryer or barrel or flat surface drying device. This may be a contnuous manufacturing process.

2. Drying can be effectuated by heat or vacuum or both.

3. In cases where drying is not necessaryk the slurry flakes may be polymerized, for instance, by infrared or ultraviolet radiation that does not degrade the drug product or other additives contained in the slurry.

4. In some cases both steps 2 and 3 may be used to manufacture the flakes.

5. In some cases, inert materials (e.g. gels, absorbents, etc.) may be used to create a flake and processed as described above. The flake may then be placed in contact with a drug so that it is

absorbed. A subsequent drying or other step (e.g. polymerization) may be necessary to complete the formation of the flake.

6. Once produced the flakes may be coated with a variety of agents for taste masking, controlled drug release, enteric release or for other purposes known by those skilled in the art of drug dosage coatings. Multiple coating Coatings may incorporate compounds such as antistatic agents. Powders or other additives may be added to the flakes to promote the pouring of flow of the flakes from containers.

E. Press, Stamp or Embossing Method

1. Flakes may be produce by injecting or flowing a slurry into or onto a mold, cavity, a plurality of cavities or embossing a thin film of slurry in such a way as to form flake-like particles. This may be a continuous process.

2. Drying and/or polymerizing the flakes may be accomplished in a similar fashion as described above in Method 1.

F. Hybrid Methods

1. Flakes may be formed by plating or printing a nucleating agent onto a surface over which you flow or expose a saturated or supersaturated liquid. When the liquid comes into contact with the nucleating agent, small crystal-like flakes are formed. The process may be stopped by removal of the liquid, for instance. The flakes may then be coated or a subsequent crystal layer may be added of the same, or different agent.

2. Flakes may be formed by preparing a slurry which is photopolymerizable or contains a photopolymerizable agent in it. As a thin film of slurry passes by, it may be exposed to a polymerizing radiation source of controlled size so that flakes are formed *in situ*.

3. Flakes may be made out of a continuous sheet of woven or nonwoven material which is saturated with a drug and cut (e.g. laser, die cut, etc.) into small flat particles.

What is claimed is: